“Efficacy of intravenous atropine to treat nausea and vomiting associated with spinal anaesthesia in patients undergoing elective caesarean section”

Thesis submitted to

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All India Institute of Medical Sciences, Bhopal

For the award of the degree of MD in the subject of

Anaesthesiology

By

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OCTOBER 2024

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by Abhinav Vijay

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AIIMS, Bhopal Institutional Human Ethics Committee- Student Research (IHEC-SR) in its 7th meeting held on 22nd February 2023 discussed your proposal titled **"Efficacy of intravenous atropine to treat nausea and vomiting associated with spinal anesthesia in patients undergoing elective caesarean section: a single arm observational study"** and evaluated it for suitability for your dissertation as required for fulfilment of MD/MS program.

Following members attended the meeting:

1. Prof. D. K. Pal, Former HoD Community Medicine, GMC, Bhopal……Chairperson
2. Prof. Rajnish Joshi, Professor of General Medicine, AIIMS, Bhopal……..Member
3. Prof. Amit Agrawal, Professor of Neurosurgery, AIIMS, Bhopal……..Member
4. Dr. Sunita Athawale, Professor of Anatomy, AIIMS, Bhopal……Member
5. Dr. Girish Bhatt, Addl. Professor of Paediatrics, AIIMS, Bhopal……..Member
6. Dr. Ujjawal Khurana, Assoc. Professor of Pathology, AIIMS, Bhopal……..Member
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9. Dr. Shashank Purwar, Professor of Microbiology, AIIMS, Bhopal……Member Secretary

The decision of the committee is as follows:

The AIIMS, Bhopal IHEC-SR approves your research protocol. All research related activities must begin only after the date of this approval. The validity of this approval is till two years from the date of issuance. Please submit a closure report / renewal request before expiration of the validity for this approval.

Shashank Purwar

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LIST OF ABBREVATIONS

ABBREVATIONS	EXPANDED FORM
IONV	Intra-operative nausea and vomiting
VAS	Visual analog scale
LSCS	Lower segment caesarean section
SAB	Sub arachnoid block
MAP	Mean arterial pressure
SVR	Systemic vascular Resistance
PPV	Positive Predictive Value
BMI	Body mass index
HR	Heart rate
BPM	Beats per minute
SBP	Systolic blood pressure
DBP	Diastolic Blood Pressure
CC	Correlation coefficient
AUC	Area under curve
NPV	Negative Predictive Value
IV	Intravenous
SD	Standard deviation
KG	Kilogram

CS	**Caesarean section**
IQR	**Interquartile range**
PONV	**Post-operative nausea and vomiting**
ECG	**Electrocardiogram**

INTRODUCTION

Spinal anesthesia is a basic procedure in modern obstetric services, especially in cesarean deliveries. It has been employed in many instances because of its effectiveness in creating a good sensory blockade with the patient remaining conscious, which may be very important in both elective and emergency surgeries(1). Spinal anesthesia is widely accepted in both developed and underdeveloped countries, speaks for its relative significance on global scale. The Royal College of Anaesthetists supports 85% as a guideline for the number of emergency cesarean sections under regional anesthesia, a fact that shows the preference of modality due to its various advantages over general anesthesia(2).

The main benefits of spinal anesthesia is that, at a cheaper cost than general anesthetic, it is linked to decreased overall rates of maternal death. The woman benefits from the spinal analgesia by being able to actively participate in the labor process while she is awake, which improves the birthing experience (2). The procedure of spinal anesthesia contirbutes for less blood loss and better postoperative pain management, critical in improving patient outcomes and recovery times.

Even with these benefits, there are drawbacks to spinal anesthesia. One common problem is the incidence of PONV and IONV, which can have a major effect on surgical results and patient comfort. Intraoperative nausea has a complex etiology that includes variables such hypotension, vagal hyperactivity, visceral pain, the usage of opioids, and the use of uterotonic drugs (4). Reports in the literature suggest that up to 80% of patients undergoing caesarean sections with subarachnoid block experience nausea and vomiting, which indicates a substantial challenge in managing these symptoms effectively (5).

Research has demonstrated that spinal anesthesia, despite its association with nausea, generally results in better neonatal outcomes than general anesthesia. According to the past researches it has been shown that neonates born via cesarean section under spinal anesthesia have higher 1-minute Apgar scores, contemplating better initial health and more favourable immediate postnatal conditions (6). This further supports the use of spinal anesthesia from neonatal wellbeing perspective.

Spinal anesthesia induced nausea and vomiting has been managed via several prophylactic and therapeutic interventions. Medication including droperidol and metoclopromide have been given to bring symptomatic relief to the patient. Droperidol is particularly effective in reducing PONV (7). Similarly, administering metoclopramide before the induction of spinal anesthesia has been found to significantly reduce both pre- and post-delivery emetic symptoms without apparent adverse effects on either the mother or the neonate (8). Another widely used antiemetic ondansetron has shown efficacy in decreasing the intensity of IONV, usually dosage of 4mg effective in reducing the symptoms (9). Also, intravenous dexamethasone in combination with intrathecal atropine is effective in embarking antiemetic action in patient undergoing cesarean section under spinal anesthesia (10).

Though it is important to note that this combination may lead to dilution of local anaesthetics, potentially affecting the quality of the sensory block.

High spinal anaesthesia, characterized by achieving a sensory level of T4 or higher, is particularly relevant for caesarean sections, as it ensures adequate blockade for the procedure (1). However, this high level of blockade can also lead to adverse physiological effects, including nausea. The predominant vagal nerve activity resulting from the sympathetic blockade can cause significant discomfort, manifesting as nausea and, occasionally, vomiting.

Atropine, an anticholinergic drug, has been identified as a potential solution for managing nausea associated with high spinal anaesthesia. Atropine acts as a competitive, reversible antagonist of muscarinic receptors, effectively blocking the vagal nerve action that is responsible for nausea (12). Although not strictly speaking an antiemetic, atropine can reduce nausea and vomiting by blocking vagal activity, which is frequently a factor in nausea brought on by anesthesia. But its principal vagolytic function takes precedence over its antiemetic actions (16). A study from 1966 showed that 0.4 mg of atropine given intravenously resulted in a 100% reduction of nausea and vomiting. Other studies have also shown the effectiveness of intravenous atropine in treating this condition (12). This study was small, however, and larger-scale validation to cover more demographics is still needed. Despite the promising evidence, research specifically focused on the efficacy of intravenous atropine in managing nausea and vomiting associated with high spinal anaesthesia remains sparse.

This study seeks to fill this gap by evaluating the effectiveness of intravenous atropine in treating these symptoms in patients undergoing elective lower segment caesarean sections under high spinal anaesthesia. By investigating this approach, the study aims to provide valuable insights into optimizing patient comfort and improving overall outcomes in this common obstetric procedure

REVIEW OF LITERATURE

- Aweke et al (2021) did a randomized control trial study at Dilla University Hospital, pregnant women scheduled for elective caesarean section were randomized to either atropine prophylaxis (n=33) or active prophylaxis (n=33) for prevention of post spinal hypotension. They concluded atropine didn't prevent a decline in blood pressure from baseline. The incidence of nausea and vomiting was lower in atropine group with no statistically significant difference. (11)

- Abdalla et al (2019) experimented with Intravenous dexamethasone combined with intrathecal atropine to prevent morphine-related nausea and vomiting after caesarean delivery. 120 parturient undergoing elective CS under spinal anaesthesia were randomized into three groups. Dexamethasone group (D): Received intrathecal hyperbaric bupivacaine (0.5% in 2 ml) mixed with morphine (200 µg in 0.5 ml) and normal saline (0.5 ml as placebo) and intravenous (iv) dexamethasone (8 mg in 2 ml). Atropine group (A): Received hyperbaric bupivacaine (0.5% in 2 ml) mixed with morphine (200 µg in 0.5 ml) and atropine (100 µg in 0.5 ml), in addition to iv normal saline (2 ml as placebo). Dexamethasone and Atropine group (DA): Received intrathecally as group A, and iv dexamethasone (8 mg in 2 ml). Follow-up of both nausea and vomiting was done during the first 24 hours postoperatively. Nausea was noticed in 7 patients (17.5%) in group D, 8 patients (20%) in group A, and one patient (2.5%) group DA, with significant differences between DA and D ($p = 0.025$) and DA and A ($p = 0.013$). Regarding vomiting, there were 5 patients

- (12.5%) in group D, 4 patients (10%) in group A only, with significant differences between DA and D ($p = 0.021$) and DA and A ($p = 0.041$). (10)

- Jelting Y. et al (2017) researched on preventing nausea and vomiting in women undergoing regional anaesthesia for caesarean section: challenges and solutions, came to conclusion that the first step for decreasing the incidence of IONV and PONV is a comprehensive management of circulatory parameters. This management includes liberal perioperative fluid administration and the application of vasopressors as the circumstances require. Antiemetic drugs may be administered restrainedly due to off-label use in pregnant women for IONV or PONV prophylaxis and may be reserved for treatment. (5)

- Vadhanan et al., 2015; atropine, a muscarinic antagonist, has been used to counteract vagally mediated bradycardia and hypotension caused by spinal anaesthesia. Studies suggest that atropine's vagolytic properties make it particularly effective in managing nausea and vomiting during high spinal anaesthesia, as it reduces parasympathetic activity

- Czarnetzki et al., 2012; Various antiemetic agents have been evaluated to manage nausea and vomiting associated with spinal anaesthesia. Ondansetron, a 5-HT3 receptor antagonist, has demonstrated efficacy in reducing both nausea and vomiting in obstetric patients.

- Jabalmeli et al (2011) conducted a study to compare efficacy of using intravenous midazolam, ondansetron, and midazolam in combination with ondansetron for treatment of nausea and vomiting after caesarean delivery in parturient underwent spinal anaesthesia. One hundred thirty-two parturients were randomly allocated to one of three groups: group M (n = 44) that received intravenous midazoalm 30 µg/kg; group O (n = 44) that received intravenous ondansetron 8 mg; group MO (n = 44) that received intravenous midazoalm 30 µg/kg combined with intravenous ondansetron 8 mg if patients had vomiting or VAS of nausea ≥ 3 during surgery (after umbilical cord clamping) and 24 hours after that. The incidence and severity of vomiting episodes and nausea with visual analogue scale (VAS) > 3 were evaluated at 2 hours, 6 hours, and 24 hours after injection of study drugs. Study showed that using intravenous midazolam 30 µg/kg in combination with intravenous ondansetron 8 mg was superior to administering single drug in treatment of emetic symptoms after caesarean delivery under spinal anaesthesia.

- Santos et al., 2009; while atropine has shown promise in reducing nausea and vomiting associated with high spinal anaesthesia, most studies in this area are dated, and sample sizes tend to be small. There is a paucity of contemporary, large-scale clinical trials assessing the safety and efficacy of atropine in this context, particularly in comparison with other antiemetic regimens such as ondansetron or dexamethasone. Additionally, the side effect profile of atropine, including potential tachycardia and dry mouth, needs to be carefully considered in obstetric populations, where maintaining maternal and fetal hemodynamics is crucial.

- Chestnut et al., 2009; despite its advantages, spinal anaesthesia is associated with a high incidence of nausea and vomiting, particularly in obstetric patients undergoing caesarean sections. Studies report an incidence as high as 60–80%, primarily due to factors such as hypotension from sympathetic blockade, visceral manipulation, and the use of uterotonic agents like oxytocin.

- Roussin et al., 2009; the incidence of nausea and vomiting is also higher when a high sensory block, such as at the T4 level, is achieved, as the higher block can lead to greater parasympathetic activity.

- Mhyre et al., 2007; spinal anaesthesia is a common technique used in caesarean sections due to its rapid onset, simplicity, and ability to provide effective sensory blockade while keeping the mother conscious during the delivery. Numerous studies have highlighted the benefits of spinal anaesthesia over general anaesthesia in obstetric settings, including lower maternal mortality, reduced systemic effects on the neonate, and decreased bleeding.

- Charbit et al., 2005; Similarly, metoclopramide and droperidol have shown some effectiveness, but concerns about side effects like sedation or extrapyramidal symptoms limit their widespread use.

- Bowring et al (2004) conducted a retrospective audit at a tertiary referral centre investigating the mode of anaesthesia and fetal outcome after emergency caesarean section. The proportion carried out under regional anaesthesia was less than recommended. Despite a longer time taken to induce anaesthesia there was no increase in adverse fetal outcome, supporting the use of regional anaesthesia wherever possible to keep maternal complications to a minimum. (2)

- Wang et al., 2000; Dexamethasone, when used as part of a multimodal antiemetic regimen, has also shown positive results in controlling postoperative nausea and vomiting (PONV)

- Ure et al in 1999 tested the hypothesis that glycopyrrolate, administered immediately before induction of subarachnoid anaesthesia for elective caesarean section, reduces the incidence and intensity of nausea and vomiting with no adverse effects on neonatal. Fifty women received either 200mcg or saline(placebo) i.v. during fluid preload, before induction of spinal anaesthesia with 2.5 ml of 0.5% isobaric bupivacaine. The intensity of nausea was assessed via a verbal scoring system and managed with increments of i.v. Ephedrine and fluids. Glycopyrrolate caused a decrease in the frequency ($p=0.02$) & severity ($p=0.03$) of nausea. It also decreased the severity of hypotension, as evidenced by decreased ephedrine requirements ($p=0.02$). No differences in neonatal Apgar scores between groups were noted.

- Abouleish et al. (1999) conducted a prospective, randomized, placebo-controlled, double-blind study to assess ondansetron efficacy during elective Caesarean section under spinal anesthesia in decreasing nausea. Seventy-four full-term pregnant females were researched. After clamping of umbilical cord, ondansetron 4 mg or 0.9% saline was given intravenously, and then studied for two hours. Nausea intensity was graded from 0 = none to 10 = maximum and vomiting was graded from single = once per minute to continuous = multiple per minute. After ondansetron, the incidence of vomiting was 36% as opposed to 58% in the control group ($p < 0.028$). Ondansetron had no effect on the frequency or intensity of nausea or vomiting. Ondansetron, however, lessened the intensity of nausea in those who reported it ($p = 0.05$). (9)
- Lussos et al (1999) 42 ASA Physical Status I–II parturients at term were randomly assigned to receive an equal volume of normal saline or 10-mg intravenous metoclopramide prior to the introduction of spinal anesthesia in a double-blind, randomized method. Compared to the control group, which saw an incidence of 14% versus 81% overall, patients in the metoclopramide-treated group experienced a considerably reduced incidence of nausea and vomiting before and after delivery. Every newborn's acid-base value was within normal ranges, and the two groups' neurobehavioral exam findings did not differ significantly. (8)

- Ayorinde et al., 1997; the parasympathetic system becomes dominant due to the blockade of sympathetic outflow, further increasing the likelihood of bradycardia and nausea. Factors such as uterine exteriorization, visceral pain, and the use of opioids also exacerbate these symptoms.

- Ratcliffe et al (1993) studied neonatal wellbeing after elective caesarean delivery with general, spinal, and epidural anaesthesia. A comparison was made of the acid-base and Apgar status of neonates following general (n = 34), spinal (n = 28) and epidural (n = 23) anaesthesia for elective caesarean section. Neonates delivered following spinal anaesthesia were more acidaemic (pH = 7.249) ($P < 0.05$) than those delivered following epidural (pH = 7.291) or general anaesthesia (pH = 7.296) despite measures taken to minimize hypotension. The percentage of neonates with a 1 min Apgar score > or = 7 was 96% after epidural anaesthesia, 93% after spinal anaesthesia and 75% after general anaesthesia. The difference between epidural and general anaesthesia was significant ($P < 0.05$). Using these two measures of neonatal wellbeing, epidural anaesthesia provided the most favourable outcome. (6)

- Tarkkila et al (1991) studied Complications during spinal anesthesia were studied prospectively in 1881 patients. Twenty-six percent of the patients suffered from one or more complications. The most common complications were hypotension (16.4%) and bradycardia (8.9%). The risk for hypotension was found to be higher with increasing age of patients (p less than 0.005). Higher peak sensory level significantly increased the risk for hypotension (p less than 0.0001), bradycardia (p

- less than 0.0001) and nausea (p less than 0.0001). Female patients suffered significantly more hypotension (p less than 0.001), nausea (p less than 0.001) and vomiting (p less than 0.001) than males. (13)

- Libersa et al. (1988) examined in 22 patients the outcomes of an intravenous single-blind infusion of ipratropium bromide against atropine sulfate. For three days, these patients were the subject of a continuous Holter recording study. A continuous saline intravenous infusion was supplemented with boluses of atropine (0.03 mg/kg) and ipratropium bromide (0.03 mg/kg) on the second and third nights (while the patient was asleep). Precise ECG interpretation made it possible to ascertain the maximum heart rate peak, when it occurred, changes in sinus cycle duration, atrioventricular conduction, and the length of time that a medication was effective. Patients were given a non-suggestive questionnaire to help identify potential side effects. When using ipratropium bromide, the mean maximum heart rate increased significantly by +46.2% and +57.4%. The duration of ipratropium bromide's effects on heart rate was almost twice that of atropine's (pharmacological half-lives of 120 +/- 38.4 min and 70 +/- 30 min, respectively). Dry mouth, a common minor muscarinic side effect, was observed with both medications. This comparative intraindividual investigation concluded that intravenous ipratropium bromide has extended vagolytic effects and may be useful in treating patients with vagally mediated automaticity and conduction abnormalities. (20)

- Santos et al (1984) studied prophylactic use of droperidol for control of nausea and vomiting during spinal anaesthesia for caesarean section. The incidence of nausea was 12% in droperidol treated patients and 40% in saline treated patients, vomiting did not occur in the droperidol group but it did in 12% of saline treated group. (7)

- Corke et al., 1982 ; the pathophysiology of nausea and vomiting in the context of spinal anaesthesia is multifactorial. Hypotension caused by sympathetic blockade is a well-recognized cause. When the block extends to the thoracic levels (T4 or higher), it causes vasodilation and reduces venous return, leading to hypotension and subsequent nausea

- Ward et al (1966) studied the experimental evaluation of atropine and other vasopressors in high spinal anaesthesia where 50 adult healthy individuals were studied while fasting and unmedicated, age group ranging from 21-40. Atropine was administered in 16 volunteers out of 50, they observed that atropine was universally effective in reducing symptoms of nausea and vomiting while ephedrine and methoxamine were ineffective. (12)

AIM AND OBJECTIVES

Aim

To evaluate the efficacy of intravenous atropine to treat nausea and vomiting associated with spinal anaesthesia in parturient females undergoing elective caesarean section.

Objectives

Primary objective

Our primary objective is to evaluate the decrease in visual analogue scale (VAS) of nausea and vomiting associated with spinal anaesthesia in parturients after administering intravenous atropine.

Secondary objectives

Our secondary objective is to

1) To measure hemodynamic changes with intravenous atropine (heart rate, blood pressure)
2) To measure the duration of action of the antiemetic effect
3) Any other discomfort due to drug administration (dryness of mouth, visual disturbances etc)

MATERIAL AND METHODS

Study design

Longitudinal study: single arm observational study

Study population: pregnant female posted for elective caesarean section

Eligibility criteria

Inclusion criteria:

ASA II-III parturients undergoing elective LSCS under subarachnoid block in whom T6 or above level of Anaesthesia will be achieved and parturients complains of nausea and/or vomiting intraoperatively.

Study Intervention: 0.4 mg intravenously atropine administration to address the complaints of nausea and/ or vomiting intraoperatively.

Exclusion criteria

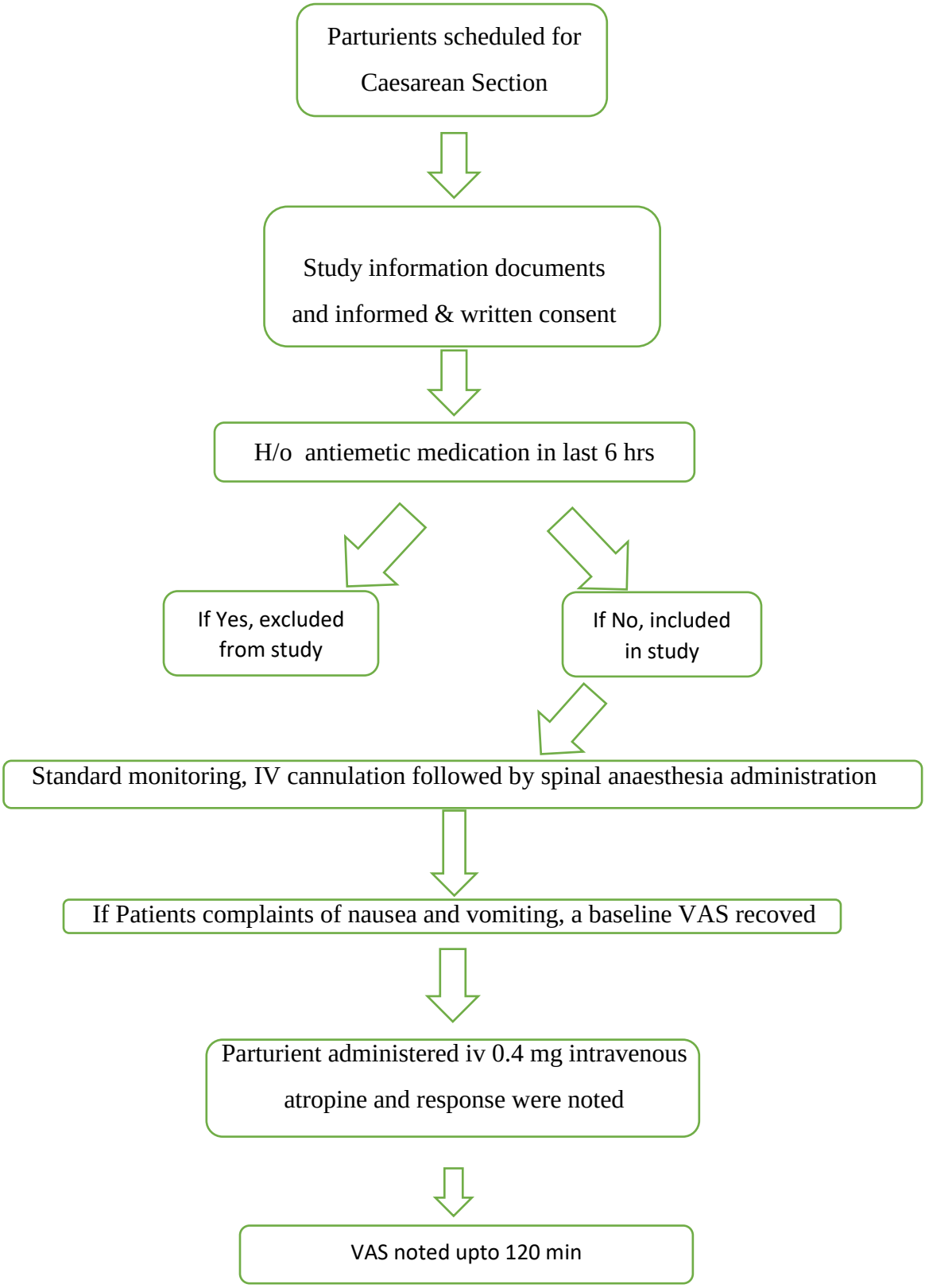
1) Non-consenting patients
2) Drug hypersensitivity to atropine or ondansetron
3) Patients who already received anti-emetic/s within previous 6 hours
4) Patient having previous history of pre-eclampsia, eclampsia or hyperemesis gravidarum
5) Patients heart rate more than 120 beats/minute at the time of atropine administration
6) Patients undergoing elective caesarean section under general anaesthesia
7) Patients with bradycardia who already received atropine
8) Cognitively impaired
9) Age <18 years

METHODOLOGY

This study was a single-arm observational trial conducted in a tertiary care setup. All patients scheduled for elective caesarean sections who were willing to participate were included, while those with a recent history of antiemetic intake within the preceding six hours were excluded. Two days prior to the scheduled operation, patients were provided with an information sheet, and written informed consent was obtained. Fasting guidelines were followed as per institutional protocol. In the operating theatre, patients were monitored using non-invasive blood pressure (NIBP), pulse oximetry, and a 5-lead electrocardiogram (ECG), with baseline blood pressure, heart rate, and oxygen saturation recorded. Blood pressure was monitored at three-minute intervals throughout the procedure. Under strict aseptic conditions, spinal anaesthesia was administered with 1.8 to 2.2 ml of 0.5% (w/v) heavy bupivacaine using a 25-gauge Quincke tip needle, with the patient in a sitting position. A wedge was placed under the patient's right hip to achieve an angle of approximately 150° or 10 cm.

If the mean arterial pressure (MAP) fell below 20% of baseline, intravenous phenylephrine in 50-microgram boluses was administered to maintain MAP within this range. Patients who achieved at least a T6 sensory block and experienced symptoms of nausea and vomiting were included in the study. Intravenous fluids were administered at a rate of 100 ml/hour. After the delivery of the fetus and the clamping of the umbilical cord, symptomatic patients received 0.4 mg of atropine. A single ampoule of atropine, containing 0.6 mg, was diluted to 10 ml in a syringe, and 6.7 ml (0.4 mg) was administered over 10 seconds following the cord clamping. In cases of twin gestation, atropine was administered after the second fetus's cord was clamped, provided the mother experienced nausea or vomiting.

Nausea and vomiting were assessed using the Visual Analogue Scale (VAS), a 10-cm horizontal line where the left end represented ‘no nausea’ and the right end represented the ‘worst imaginable nausea.’ Patients marked the severity of their nausea by indicating a point on the line, which was measured in centimeters from the left to quantify the intensity of their symptoms. Any episode of nausea or vomiting occurring within two hours of spinal anaesthesia administration was treated with atropine. If nausea or vomiting persisted after atropine administration, intravenous ondansetron 4 mg was given slowly over four minutes as a rescue treatment, with a maximum allowable dose of 8 mg of ondansetron.


Parturients scheduled for Caesarean Section
Study information documents and informed & written consent
H/o antiemetic medication in last 6 hrs
If Yes, excluded from study
If No, included in study
Standard monitoring, IV cannulation followed by spinal anaesthesia administration
If Patients complaints of nausea and vomiting, a baseline VAS recoved
Parturient administered iv 0.4 mg intravenous atropine and response were noted
VAS noted upto 120 min

DATA ANALYSIS

SAMPLE SIZE CALCULATION

Since we are calculating the efficacy of atropine in the above-mentioned regard and in the past not enough literature is found we will take proportion of unknown which is 0.50.

We have calculated sample size using web-based sample size calculator {Arifin, W.N. (2023)}. Sample size calculator (web). Retrieved from wnarifin.github.io

Assumptions in sample size were based on all the past literature found. To estimate efficacy of 50% with 95% confidence interval of 30 to 70%(precision of 0.2), and 20% non-response rate, required minimum sample size is 32

But the sample size was increased to 60 due to number elective LSCS in our institution increased. So as to increase the validity, the sample size was taken as 60

Observation and Results

This section presents the observations and results derived from the analysis of 60 patients we recruited for our study. The study focused on monitoring key parameters such as nausea/vomiting scores using the Visual Analogue Scale (VAS), systolic and diastolic blood pressure, mean arterial pressure (MAP), heart rate, and the level of spinal anesthesia. These metrics were recorded at baseline just before administration of atropine and at various intervals throughout the surgical procedure and recovery.

Table 1: Summary of Demographic details

Basic Details	**Mean ± SD || Median (IQR) || Min-Max OR N (%)**
Age (Years)	28.83 ± 4.50 || 28.00 (26.00-32.00) || 20.00 - 39.00
Age	
20-29 Years	36 (60.0%)
30-39 Years	24 (40.0%)
Weight (Kg)	69.48 ± 11.22 || 69.00 (60.00-79.00) || 50.00 - 90.00
Height (cm)	157.98 ± 5.48 || 158.00 (153.00-162.00) || 150.00 - 170.00
BMI (Kg/m^2)	27.77 ± 3.82 || 27.42 (24.55-30.89) || 21.37 - 35.41

OBSERVATIONS AND RESULTS

The mean Age (Years) was 28.83 ± 4.50.

36 (60.0%) of the participants had Age: 20-29 Years. 24 (40.0%) of the participants had Age: 30-39 Years.

The mean Weight (Kg) was 69.48 ± 11.22.

The mean Height (cm) was 157.98 ± 5.48.

The mean BMI (Kg/m²) was 27.77 ± 3.82

Table 2: Assessment of VAS of nausea and vomiting after atropine administration

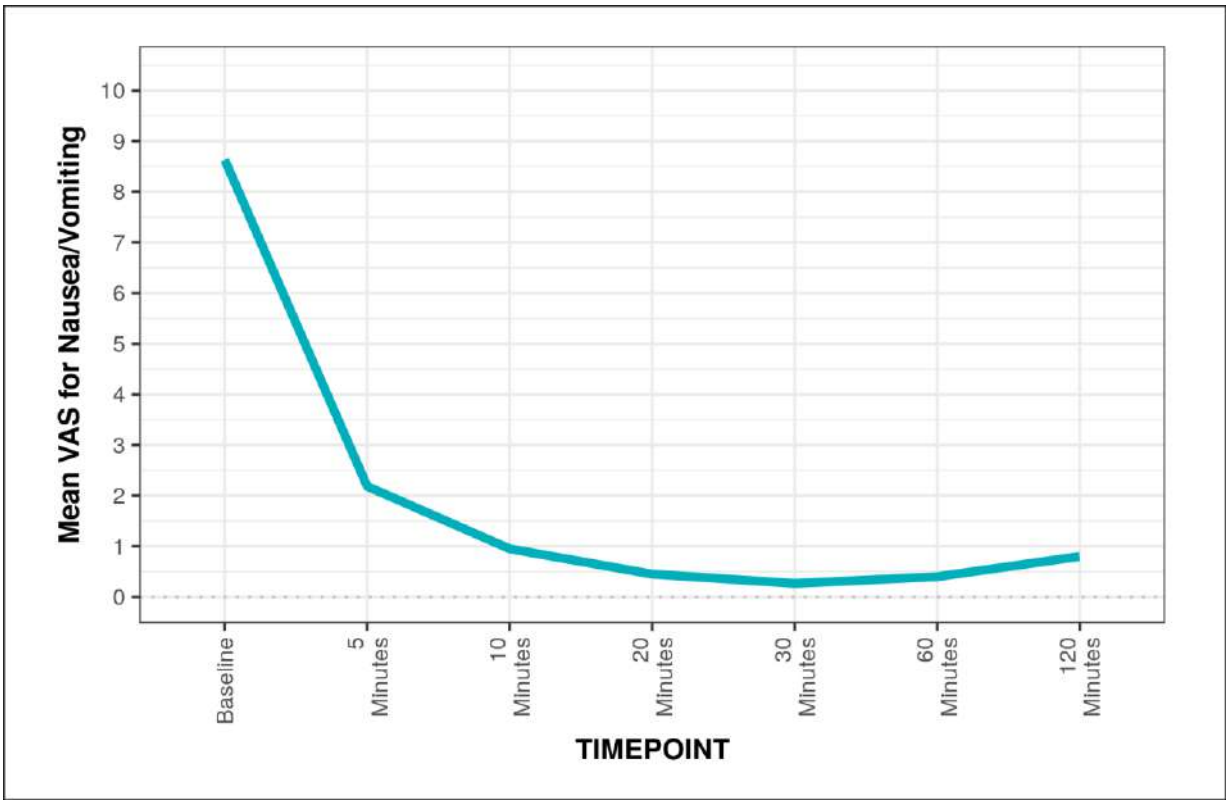
Timepoint	VAS for Nausea/Vomiting			Friedman Test	
	Mean (SD)	Median (IQR)	Range	$\chi 2$	P Value
Baseline	8.63 (1.26)	8.00 (2.00)	6.00 - 10.00	255.5	<0.001
5 Minutes	2.18 (2.33)	2.00 (4.00)	0.00 - 8.00		
10 Minutes	0.95 (1.61)	0.00 (2.00)	0.00 - 6.00		
20 Minutes	0.45 (1.16)	0.00 (0.00)	0.00 - 5.00		
30 Minutes	0.27 (0.84)	0.00 (0.00)	0.00 - 5.00		
60 Minutes	0.40 (1.01)	0.00 (0.00)	0.00 - 5.00		
120 Minutes	0.80 (1.33)	0.00 (2.00)	0.00 - 5.00		

Non-parametric tests (Friedman test) were used to make statistical inference as data were not normally distributed. Friedman test was used to explore whether the VAS for Nausea/Vomiting changed significantly over time.

The mean VAS for Nausea/Vomiting decreased from a maximum of 8.63 at the Baseline timepoint to a minimum of 0.27 at the 30 Minutes timepoint, and then increased to 0.80 at

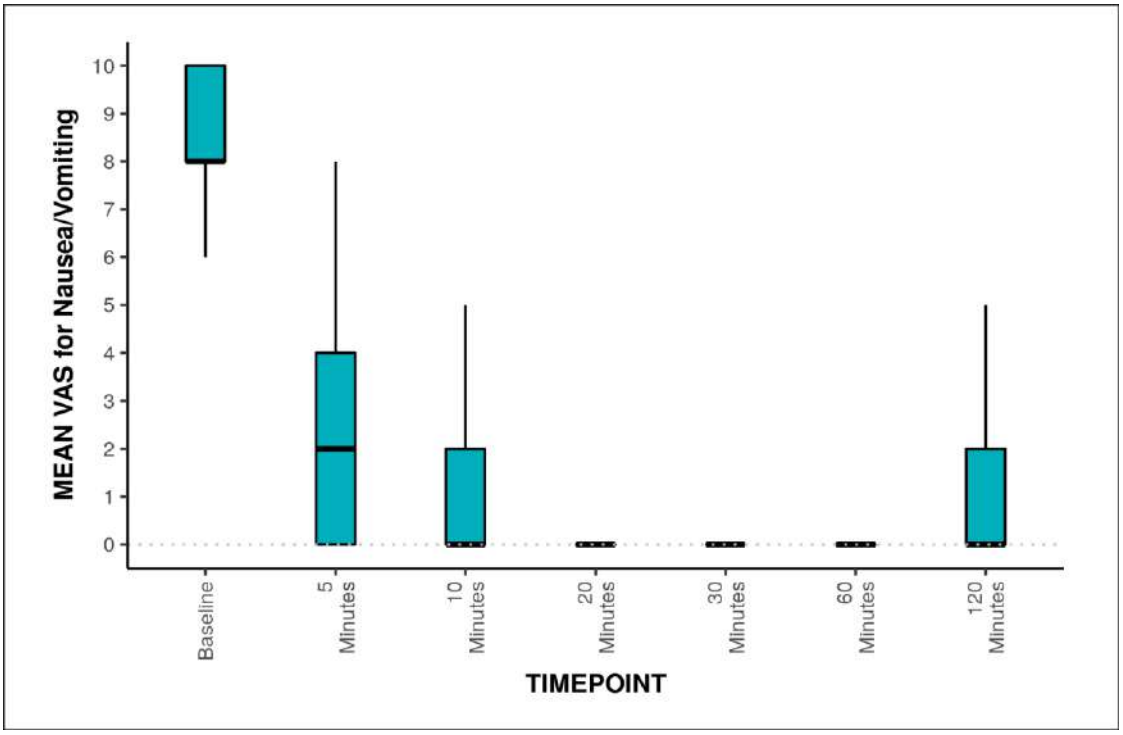
the 120 Minutes timepoint. This change was statistically significant (Friedman Test: $\chi 2$ = 255.5, p = <0.001).

Figure 1: Line diagram depicting Change in VAS for Nausea/Vomiting Over Time



The Box-and-Whisker plot below depicts the distribution of VAS for Nausea/Vomiting over different timepoints. In each box, the middle horizontal line represents the median VAS for Nausea/Vomiting, the upper and lower bounds of the box represent the 75th and the 25th centile of VAS for Nausea/Vomiting respectively, and the upper and lower extent of the whiskers represent the Tukey limits for VAS for Nausea/Vomiting at each of the timepoints respectively.

Figure 2: Box-and-whisker plot depicting change in VAS for Nausea/Vomiting Over Time



Post-hoc pairwise analysis was performed to explore at which timepoints the VAS for Nausea/Vomiting differed significantly from the Baseline timepoint

Table 3: Summarizes analysis of timepoints at which VAS Nausea/Vomiting differed significantly:

Comparison of VAS for Nausea/Vomiting at Various Timepoints vs Baseline	Mean (SD) of Difference	Median (IQR) of Difference	Range of Difference	p value
5 Minutes - Baseline	-6.45 (2.55)	-6.00 (3.00)	-10.00 - -2.00	<0.001
10 Minutes - Baseline	-7.68 (1.92)	-8.00 (4.00)	-10.00 - -2.00	<0.001
20 Minutes - Baseline	-8.18 (1.62)	-8.00 (3.00)	-10.00 - -4.00	<0.001
30 Minutes - Baseline	-8.37 (1.43)	-8.00 (2.00)	-10.00 - -4.00	<0.001
60 Minutes - Baseline	-8.23 (1.57)	-8.00 (3.00)	-10.00 - -4.00	<0.001
120 Minutes - Baseline	-7.83 (1.80)	-8.00 (3.00)	-10.00 - -4.00	<0.001

Post-Hoc pairwise tests for Friedman test performed using Nemenyi Test method for p value correction. Green background denotes statistically significant difference at $p < 0.05$.

The VAS for Nausea/Vomiting differed significantly from the Baseline timepoint at the following timepoints: 5 Minutes, 10 Minutes, 20 Minutes, 30 Minutes, 60 Minutes, 120 Minutes.

The maximum change from the Baseline timepoint was observed at the 30 Minutes timepoint.

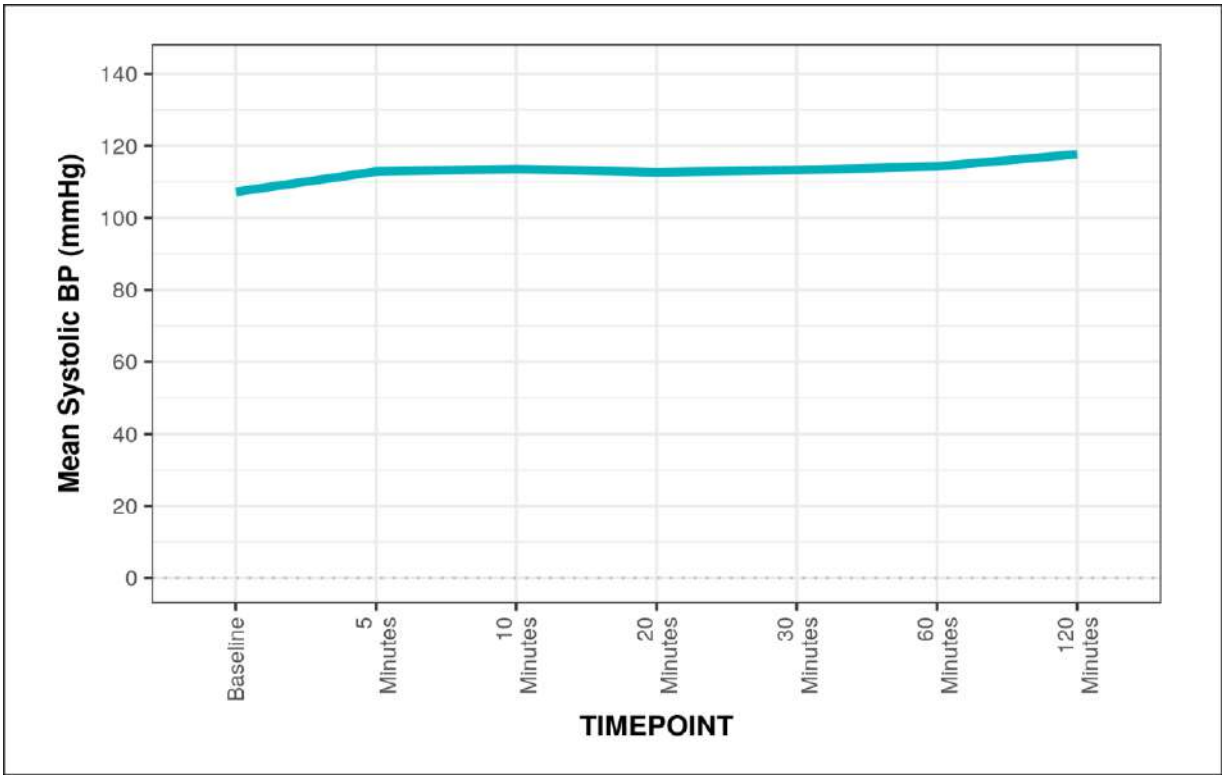
Table 4: Assessment of systolic BP (mmHg) over time

Timepoint	Systolic BP (mmHg)			Friedman Test	
	Mean (SD)	Median (IQR)	Range	$\chi 2$	P Value
Baseline	107.22 (8.82)	108.00 (9.25)	90.00 - 143.00	76.2	<0.001
5 Minutes	112.88 (8.82)	112.00 (9.25)	98.00 - 146.00		
10 Minutes	113.58 (8.43)	114.50 (8.00)	94.00 - 138.00		
20 Minutes	112.67 (7.80)	112.00 (9.25)	90.00 - 140.00		
30 Minutes	113.30 (9.80)	112.00 (10.25)	92.00 - 155.00		
60 Minutes	114.30 (8.65)	112.50 (8.00)	95.00 - 154.00		
120 Minutes	117.68 (6.89)	117.50 (8.25)	98.00 - 146.00		

Non-parametric tests (Friedman test) were used to make statistical inference as data were not normally distributed. Friedman test was used to explore whether the Systolic BP (mmHg) changed significantly over time.

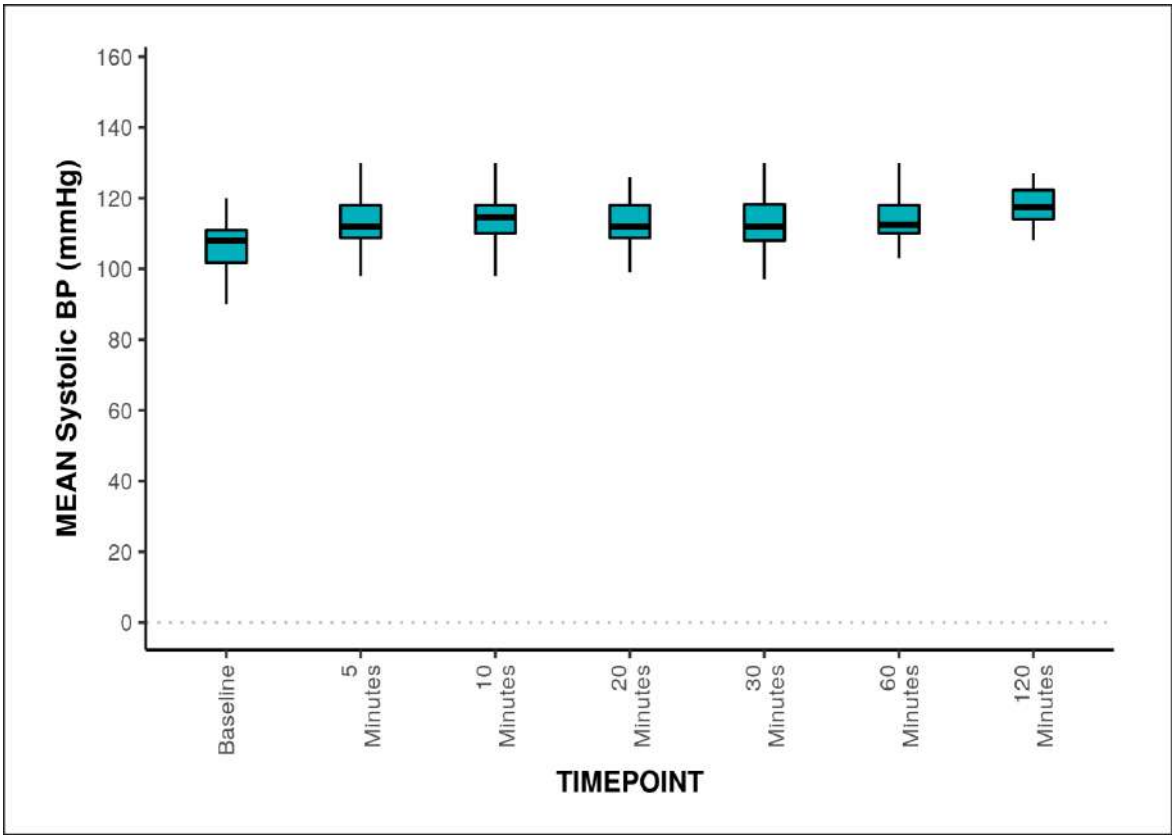
The mean Systolic BP (mmHg) increased from a minimum of 107.22 at the Baseline timepoint to a maximum of 117.68 at the 120 Minutes timepoint. This change was statistically significant (Friedman Test: $\chi 2 = 76.2$, $p = <0.001$).

Figure 3: Line diagram depicting change in Systolic BP (mmHg) Over Time



The Box-and-Whisker plot below depicts the distribution of Systolic BP (mmHg) over different timepoints. In each box, the middle horizontal line represents the median Systolic BP (mmHg), the upper and lower bounds of the box represent the 75th and the 25th centile of Systolic BP (mmHg) respectively, and the upper and lower extent of the whiskers represent the Tukey limits for Systolic BP (mmHg) at each of the timepoints respectively.

Figure 4: Box-and-whisker plot depicting change in Systolic BP (mmHg) Over Time



Post-hoc pairwise analysis was performed to explore at which timepoints the Systolic BP (mmHg) differed significantly from the Baseline timepoint.

Table 5: Summarizes analysis of timepoints where systolic BP (mmHg) differed significantly:

Comparison of Systolic BP (mmHg) at Various Timepoints vs Baseline	Mean (SD) of Difference	Median (IQR) of Difference	Range of Difference	p value
5 Minutes - Baseline	5.67 (7.10)	5.50 (9.50)	-13.00 - 25.00	<0.001
10 Minutes - Baseline	6.37 (7.48)	6.00 (8.25)	-6.00 - 30.00	<0.001
20 Minutes - Baseline	5.45 (7.45)	5.50 (8.50)	-9.00 - 28.00	0.001
30 Minutes - Baseline	6.08 (8.95)	7.50 (10.50)	-23.00 - 21.00	<0.001
60 Minutes - Baseline	7.08 (7.83)	6.00 (10.00)	-19.00 - 26.00	<0.001
120 Minutes - Baseline	10.47 (8.75)	9.50 (11.25)	-17.00 - 36.00	<0.001

Post-Hoc pairwise tests for Friedman test performed using Nemenyi Test method for p value correction. Green background denotes statistically significant difference at $p < 0.05$.

The Systolic BP (mmHg) differed significantly from the Baseline timepoint at the following timepoints: 5 Minutes, 10 Minutes, 20 Minutes, 30 Minutes, 60 Minutes, 120 Minutes.

The maximum change from the Baseline timepoint was observed at the 120 Minutes timepoint.

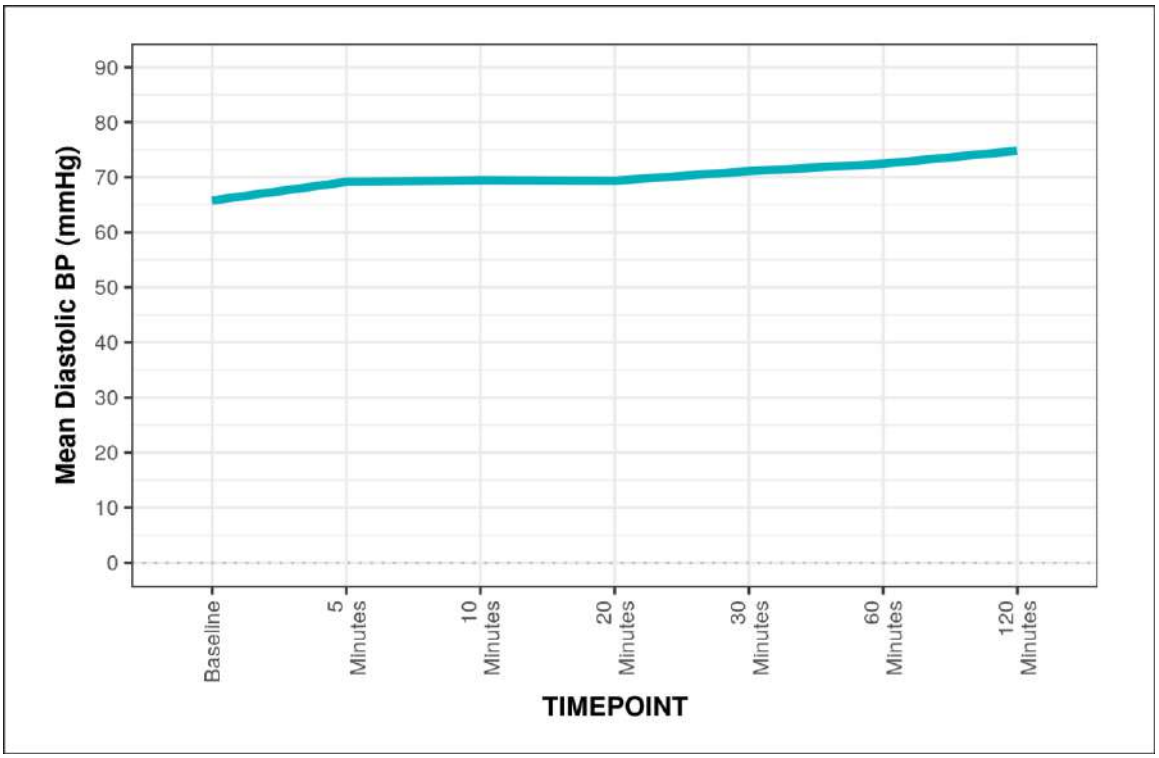
Table 6: Assessment of diastolic BP (mmHg) over time

Timepoint	Diastolic BP (mmHg)			Friedman Test	
	Mean (SD)	Median (IQR)	Range	$\chi 2$	P Value
Baseline	65.78 (7.21)	65.00 (8.25)	52.00 - 96.00	93.6	<0.001
5 Minutes	69.15 (8.53)	69.00 (7.00)	49.00 - 109.00		
10 Minutes	69.47 (7.63)	68.00 (9.00)	57.00 - 98.00		
20 Minutes	69.38 (5.86)	70.00 (7.00)	54.00 - 90.00		
30 Minutes	71.10 (8.63)	70.00 (8.25)	57.00 - 111.00		
60 Minutes	72.45 (7.49)	71.00 (6.50)	59.00 - 101.00		
120 Minutes	74.80 (6.35)	74.50 (7.50)	62.00 - 98.00		

Non-parametric tests (Friedman test) were used to make statistical inference as data were not normally distributed. Friedman test was used to explore whether the Diastolic BP (mmHg) changed significantly over time.

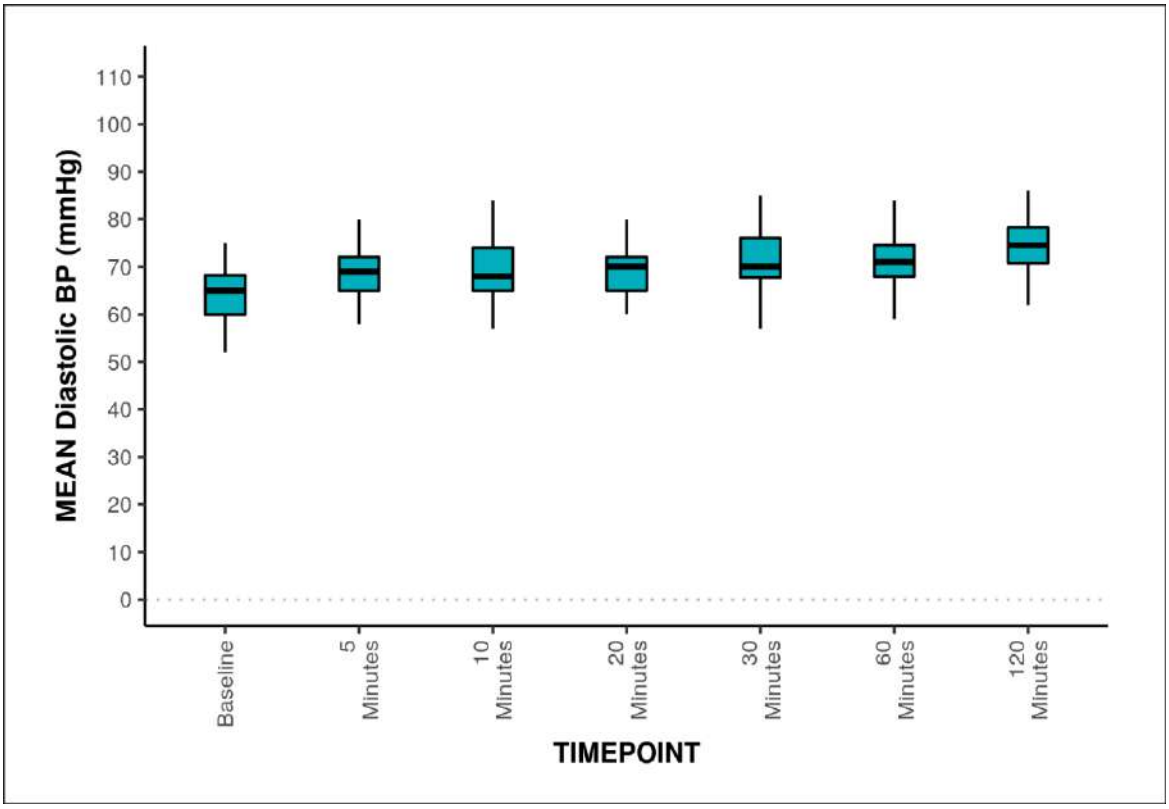
The mean Diastolic BP (mmHg) increased from a minimum of 65.78 at the Baseline timepoint to a maximum of 74.80 at the 120 Minutes timepoint. This change was statistically significant (Friedman Test: $\chi 2 = 93.6$, $p = <0.001$).

Figure 5: Line diagram depicting change in Diastolic BP (mmHg) Over Time



The Box-and-Whisker plot below depicts the distribution of Diastolic BP (mmHg) over different timepoints. In each box, the middle horizontal line represents the median Diastolic BP (mmHg), the upper and lower bounds of the box represent the 75th and the 25th centile of Diastolic BP (mmHg) respectively, and the upper and lower extent of the whiskers represent the Tukey limits for Diastolic BP (mmHg) at each of the timepoints respectively.

Figure 6: Box-and-whisker plot depicting change in Diastolic BP (mmHg) Over Time



Post-hoc pairwise analysis was performed to explore at which timepoints the Diastolic BP (mmHg) differed significantly from the Baseline timepoint.

Table 7: Summarizes analysis of timepoints at which diastolic BP differed significantly:

Comparison of Diastolic BP (mmHg) at Various Timepoints vs Baseline	Mean (SD) of Difference	Median (IQR) of Difference	Range of Difference	p value
5 Minutes - Baseline	3.37 (7.25)	4.50 (7.50)	-26.00 - 18.00	0.024
10 Minutes - Baseline	3.68 (7.53)	3.50 (9.50)	-13.00 - 20.00	0.024
20 Minutes - Baseline	3.60 (6.55)	3.00 (8.50)	-8.00 - 20.00	0.017
30 Minutes - Baseline	5.32 (7.71)	5.00 (9.25)	-14.00 - 21.00	<0.001
60 Minutes - Baseline	6.67 (7.39)	7.00 (8.00)	-15.00 - 30.00	<0.001
120 Minutes - Baseline	9.02 (8.09)	9.00 (8.00)	-12.00 - 34.00	<0.001

Post-Hoc pairwise tests for Friedman test performed using Nemenyi Test method for p value correction. Green background denotes statistically significant difference at $p < 0.05$.

The Diastolic BP (mmHg) differed significantly from the Baseline timepoint at the following timepoints: 5 Minutes, 10 Minutes, 20 Minutes, 30 Minutes, 60 Minutes, 120 Minutes.

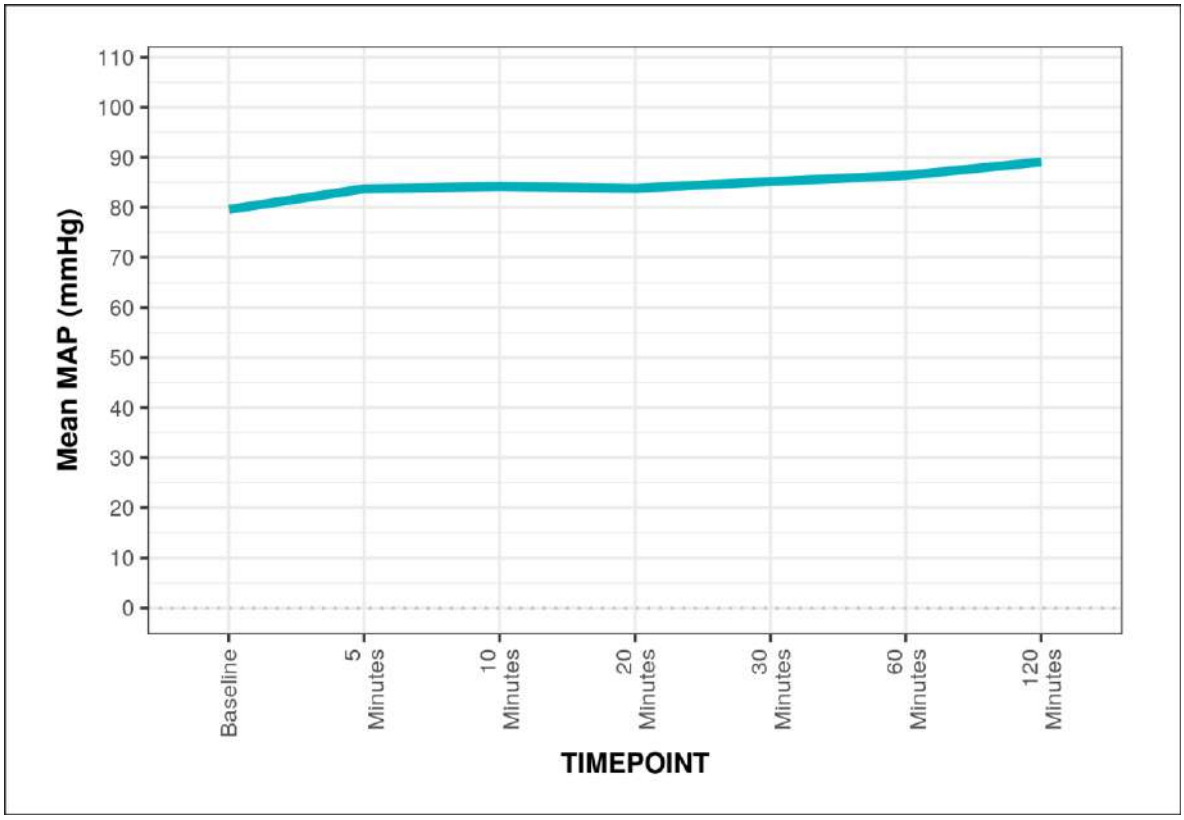
The maximum change from the Baseline timepoint was observed at the 120 Minutes timepoint

Table 8: Assessment of change in MAP (mmHg) over time

Timepoint	MAP (mmHg)			Friedman Test	
	Mean (SD)	Median (IQR)	Range	$\chi 2$	P Value
Baseline	79.59 (6.77)	79.33 (6.83)	68.00 - 111.67	118.3	<0.001
5 Minutes	83.73 (7.56)	82.67 (6.92)	69.00 - 121.33		
10 Minutes	84.17 (6.70)	83.67 (9.17)	71.33 - 111.33		
20 Minutes	83.81 (5.58)	84.33 (6.83)	72.67 - 106.67		
30 Minutes	85.17 (8.04)	84.50 (7.67)	71.67 - 125.67		
60 Minutes	86.40 (6.90)	85.33 (8.08)	76.67 - 118.67		
120 Minutes	89.09 (5.72)	88.67 (5.83)	80.67 - 114.00		

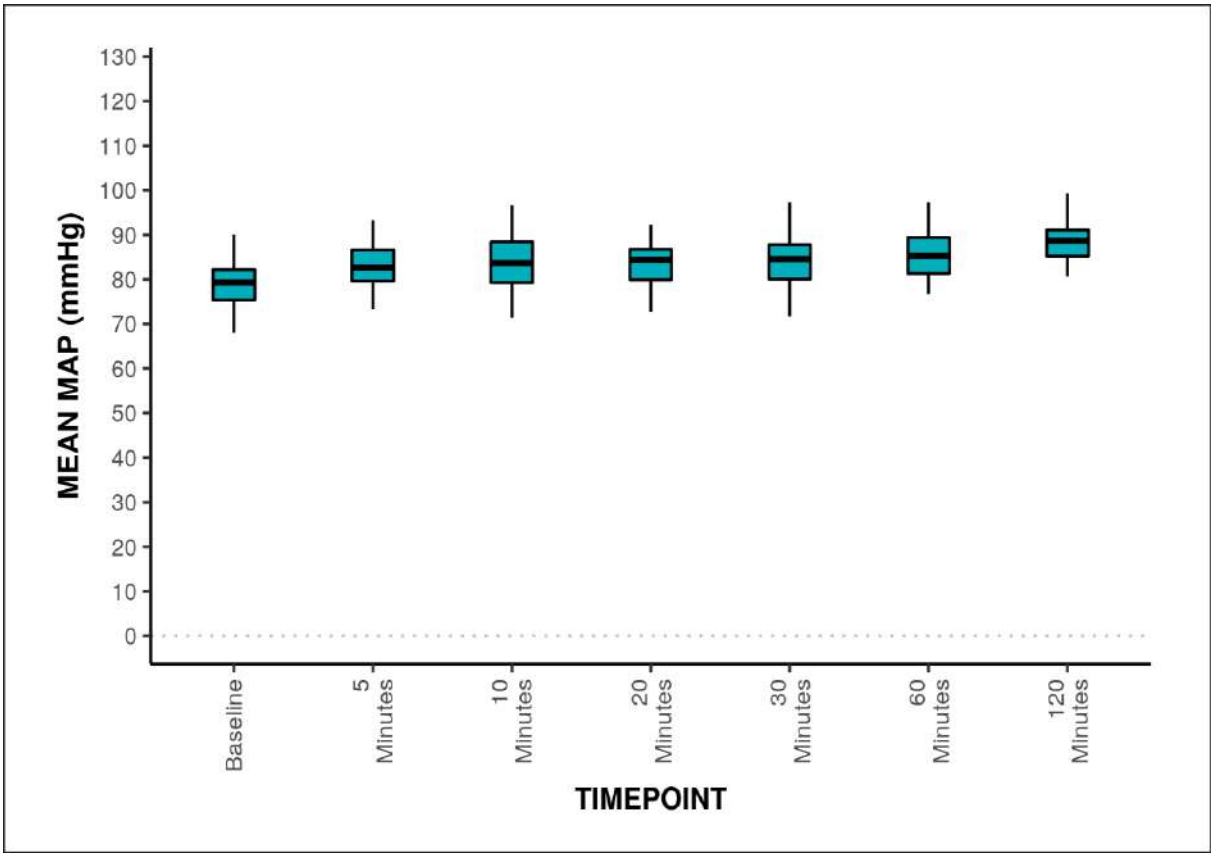
Non-parametric tests (Friedman test) were used to make statistical inference as data were not normally distributed. Friedman test was used to explore whether the MAP (mmHg) changed significantly over time. The mean MAP (mmHg) increased from a minimum of 79.59 at the Baseline timepoint to a maximum of 89.09 at the 120 Minutes timepoint. This change was statistically significant (Friedman Test: $\chi 2 = 118.3$, $p = <0.001$).

Figure 7: Line diagram depicting change in MAP (mmHg) Over Time



The Box-and-Whisker plot below depicts the distribution of MAP (mmHg) over different timepoints. In each box, the middle horizontal line represents the median MAP (mmHg), the upper and lower bounds of the box represent the 75th and the 25th centile of MAP (mmHg) respectively, and the upper and lower extent of the whiskers represent the Tukey limits for MAP (mmHg) at each of the timepoints respectively.

Figure 8: Box-and-whisker plot depicting change in MAP (mmHg) Over Time



Post-hoc pairwise analysis was performed to explore at which timepoints the MAP (mmHg) differed significantly from the Baseline timepoint.

Table 9: Summarizes analysis of timepoints at which MAP differed significantly:

Comparison of MAP (mmHg) at Various Timepoints vs Baseline	Mean (SD) of Difference	Median (IQR) of Difference	Range of Difference	p value
5 Minutes - Baseline	4.13 (5.74)	4.50 (7.75)	-18.00 - 15.33	0.001
10 Minutes - Baseline	4.58 (5.95)	4.17 (7.17)	-10.33 - 18.67	<0.001
20 Minutes - Baseline	4.22 (5.49)	4.17 (7.17)	-5.67 - 17.00	0.002
30 Minutes - Baseline	5.57 (6.37)	5.83 (6.25)	-17.00 - 20.00	<0.001
60 Minutes - Baseline	6.81 (6.24)	6.67 (5.58)	-16.33 - 24.67	<0.001
120 Minutes - Baseline	9.50 (6.65)	9.33 (6.17)	-12.33 - 31.33	<0.001

Post-Hoc pairwise tests for Friedman test performed using Nemenyi Test method for p value correction. Green background denotes statistically significant difference at $p < 0.05$.

The MAP (mmHg) differed significantly from the Baseline timepoint at the following timepoints: 5 Minutes, 10 Minutes, 20 Minutes, 30 Minutes, 60 Minutes, 120 Minutes.

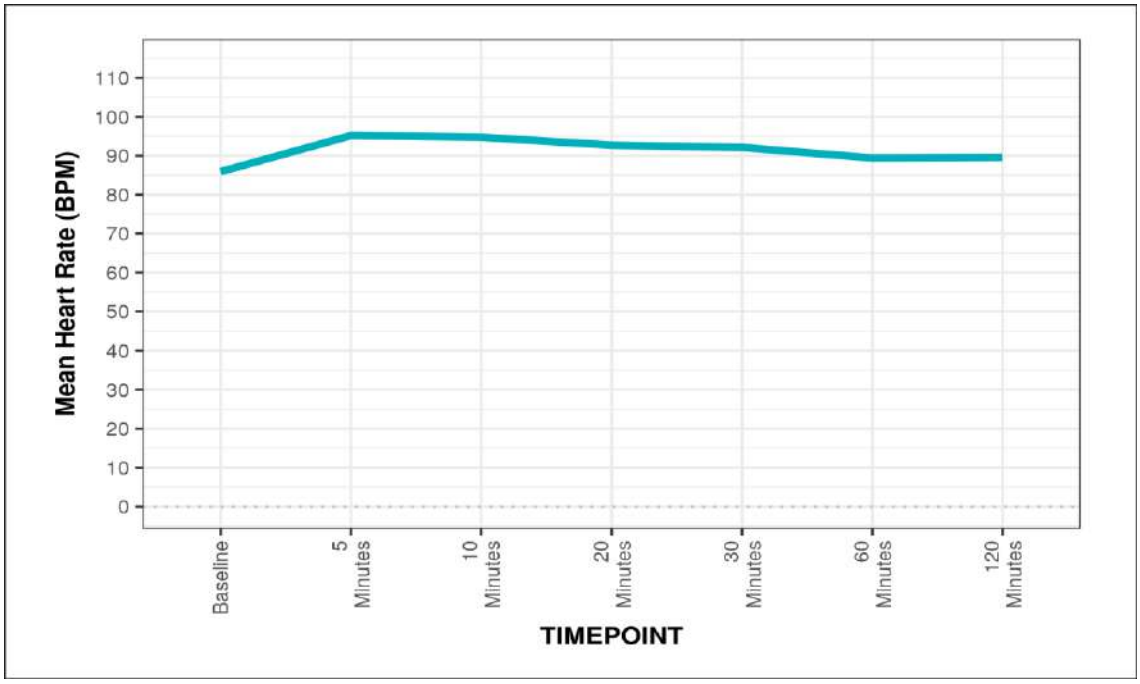
The maximum change from the Baseline timepoint was observed at the 120 Minutes timepoint.

Table 10: Assessment of change in Heart Rate (BPM) over time

Timepoint	Heart Rate (BPM)			Friedman Test	
	Mean (SD)	Median (IQR)	Range	$\chi 2$	P Value
Baseline	85.92 (12.75)	85.50 (12.50)	62.00 - 115.00	52.0	<0.001
5 Minutes	95.17 (16.71)	88.50 (28.00)	68.00 - 135.00		
10 Minutes	94.75 (16.65)	92.00 (26.50)	65.00 - 136.00		
20 Minutes	92.70 (17.38)	88.00 (24.75)	66.00 - 146.00		
30 Minutes	92.13 (16.06)	89.00 (19.25)	65.00 - 131.00		
60 Minutes	89.42 (13.50)	87.50 (18.75)	63.00 - 118.00		
120 Minutes	89.60 (11.63)	90.00 (13.50)	66.00 - 118.00		

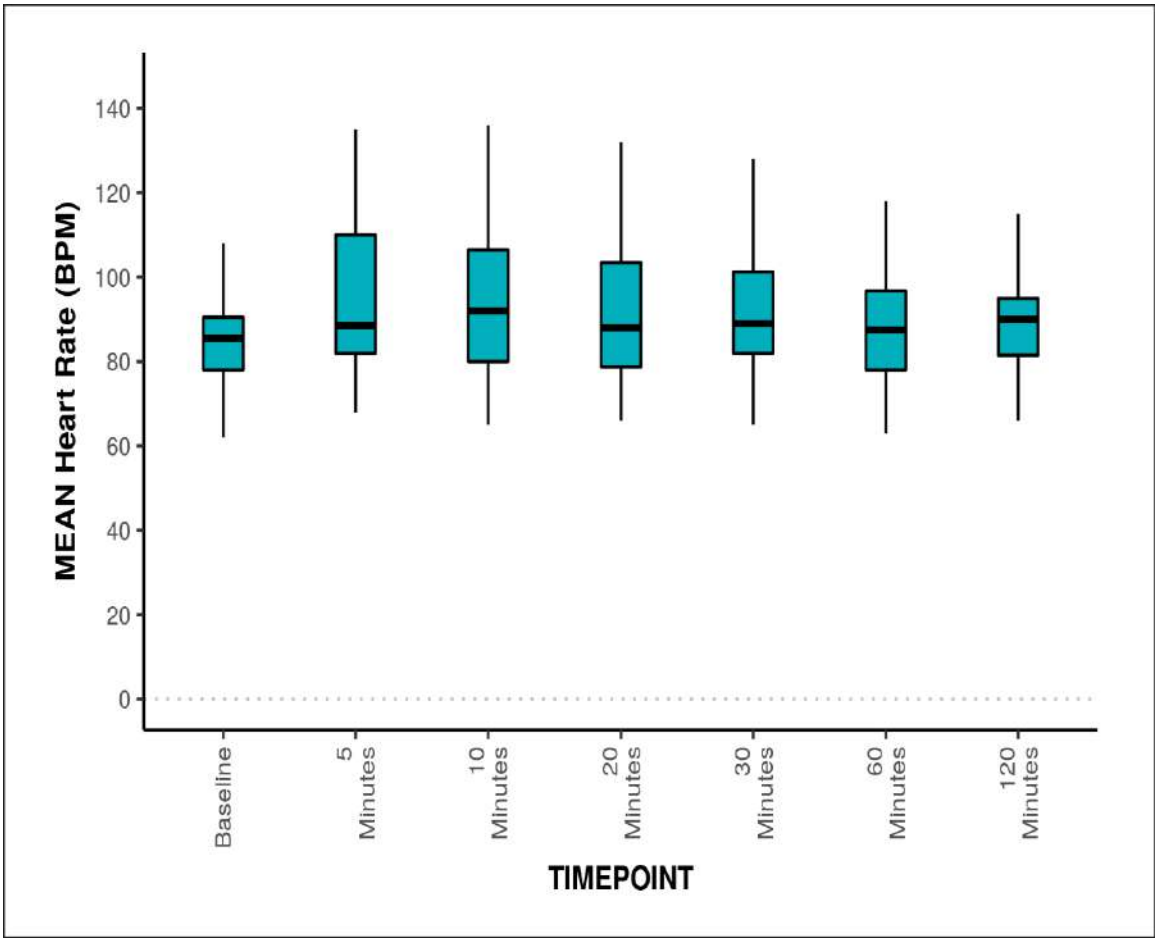
Non-parametric tests (Friedman test) were used to make statistical inference as data were not normally distributed. Friedman test was used to explore whether the Heart Rate (BPM) changed significantly over time. The mean Heart Rate (BPM) increased from a minimum of 85.92 at the Baseline timepoint to a maximum of 95.17 at the 5 Minutes timepoint, and then decreased to 89.60 at the 120 Minutes timepoint. This change was statistically significant (Friedman Test: $\chi 2 = 52.0$, $p = <0.001$).

Figure 9: Line diagram depicting change in Heart Rate (BPM) Over Time



The Box-and-Whisker plot below depicts the distribution of Heart Rate (BPM) over different timepoints. In each box, the middle horizontal line represents the median Heart Rate (BPM), the upper and lower bounds of the box represent the 75th and the 25th centile of Heart Rate (BPM) respectively, and the upper and lower extent of the whiskers represent the Tukey limits for Heart Rate (BPM) at each of the timepoints respectively.

Figure 10: Box-and-whisker depicting change in Heart Rate (BPM) Over Time



Post-hoc pairwise analysis was performed to explore at which timepoints the Heart Rate (BPM) differed significantly from the Baseline timepoint.

Table 11: Summarizes analysis of timepoints at which Heart Rate differed significantly:

Comparison of Heart Rate (BPM) at Various Timepoints vs Baseline	Mean (SD) of Difference	Median (IQR) of Difference	Range of Difference	p value
5 Minutes - Baseline	9.25 (11.50)	7.50 (10.50)	-10.00 - 49.00	<0.001
10 Minutes - Baseline	8.83 (12.78)	6.00 (13.25)	-12.00 - 51.00	<0.001
20 Minutes - Baseline	6.78 (13.50)	4.50 (13.50)	-21.00 - 48.00	0.008
30 Minutes - Baseline	6.22 (11.72)	5.50 (12.75)	-16.00 - 41.00	0.004
60 Minutes - Baseline	3.50 (9.43)	4.00 (10.25)	-13.00 - 34.00	0.608
120 Minutes - Baseline	3.68 (9.86)	4.50 (13.00)	-13.00 - 28.00	0.332

Post-Hoc pairwise tests for Friedman test performed using Nemenyi Test method for p value correction. Green background denotes statistically significant difference at $p < 0.05$.

The Heart Rate (BPM) differed significantly from the Baseline timepoint at the following timepoints: 5 Minutes, 10 Minutes, 20 Minutes, 30 Minutes.

The maximum change from the Baseline timepoint was observed at the 5 Minutes timepoint.

Table 12: Distribution of the Participants in Terms of 'Onset of Antiemesis (Minutes)'

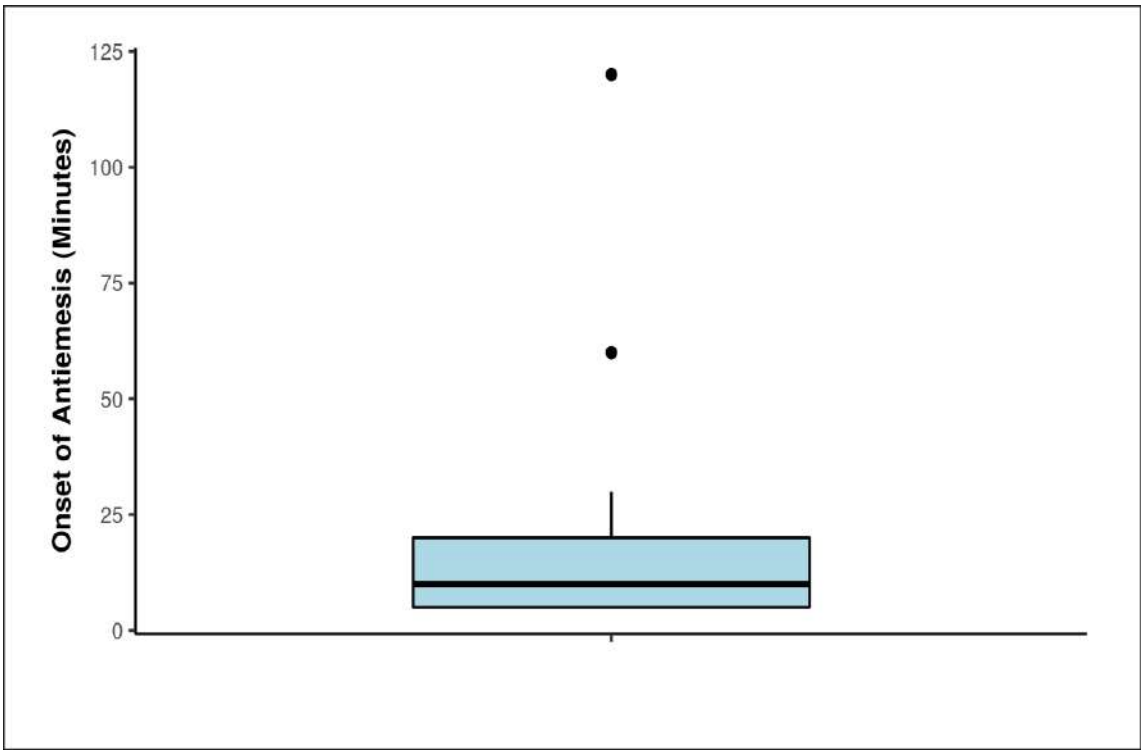
Onset of Antiemesis (Minutes)	
Mean (SD)	13.36 (17.67)
Median (IQR)	10 (5-20)
Range	5 - 120

The mean (SD) of Onset of Antiemesis (Minutes) was 13.36 (17.67). The median (IQR) of Onset of Antiemesis (Minutes) was 10.00 (5-20). The Onset of Antiemesis (Minutes) ranged from 5 - 120.

The skewness of the data was 4.33, and it suggested that the data was positively skewed, thus suggesting it was not normally distributed. The kurtosis of the data was 22.09, and it suggested that the data was not normally distributed. Shapiro-Wilk test for the data was significant ($p = <0.001$), suggesting that the data was not normally distributed. There appeared to be more than one mode/peak in the data, thus making it multimodal.

Since the data was multimodal (had more than one peak), it appeared that the data was not normally distributed (did not follow a bell-shaped curve).

Figure 11: Distribution of Onset of Antiemesis (Minutes)



The following histogram in plotted with the actual counts, and an ideal bell-shaped curve is superimposed on top for reference:

Figure 12: Distribution of Onset of Antiemesis (Minutes)

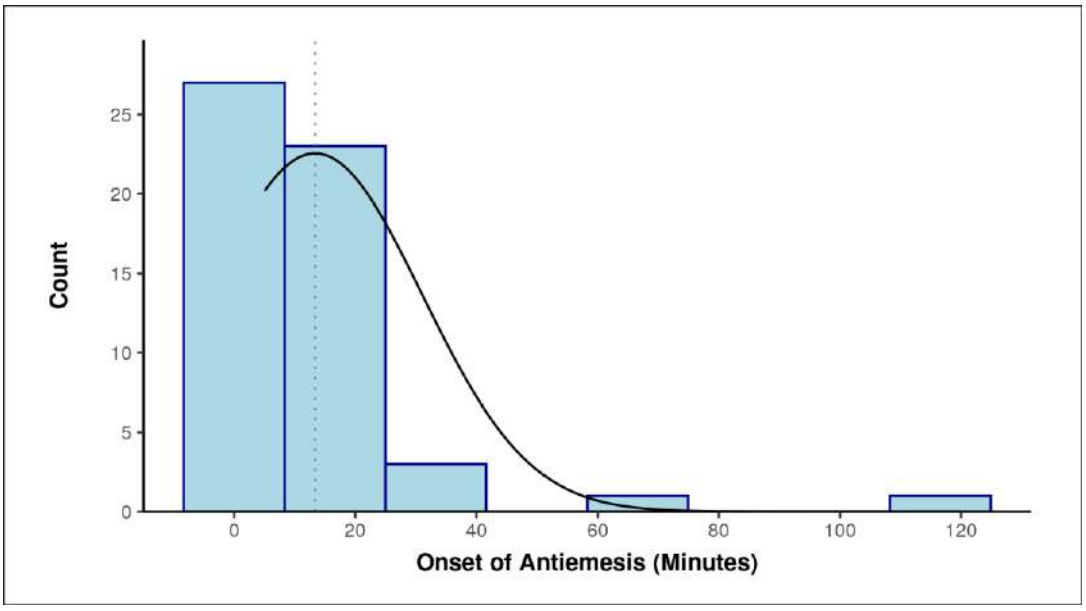


Table 13: Association between 'Effectiveness' and 'Onset of Antiemesis (Minutes)'

Onset of Antiemesis (Minutes)	Effectiveness		Wilcoxon-Mann-Whitney U Test	
	Yes	No	W	p value
Mean (SD)	13.06 (17.68)	30.00 (NA)	3.000	0.111
Median (IQR)	7.5 (5-17.5)	30 (30-30)		
Min - Max	5 - 120	30 - 30		

The variable Onset of Antiemesis (Minutes) was not normally distributed in the 2 subgroups of the variable Effectiveness. Thus, non-parametric tests (Wilcoxon-Mann-Whitney U Test) were used to make group comparisons.

The mean (SD) of Onset of Antiemesis (Minutes) in the Effectiveness: Yes group was 13.06 (17.68). The mean (SD) of Onset of Antiemesis (Minutes) in the Effectiveness: No group was 30.00 (NA). The median (IQR) of Onset of Antiemesis (Minutes) in the Effectiveness: Yes group was 7.5 (5-17.5). The median (IQR) of Onset of Antiemesis (Minutes) in the Effectiveness: No group was 30 (30-30). The Onset of Antiemesis (Minutes) in the Effectiveness: Yes ranged from 5 - 120. The Onset of Antiemesis (Minutes) in the Effectiveness: No ranged from 30 - 30.

There was no significant difference between the groups in terms of Onset of Antiemesis (Minutes) ($W = 3.000$, $p = 0.111$).

Strength of Association (Point-Biserial Correlation) = 0.13 (Small Effect Size)

The Box-and-Whisker plot below depicts the distribution of Onset of Antiemesis (Minutes) in the 2 groups. The middle horizontal line represents the median Onset of Antiemesis (Minutes), the upper and lower bounds of the box represent the 75th and the 25th centile of Onset of Antiemesis (Minutes) respectively, and the upper and lower extent of the whiskers represent the Tukey limits for Onset of Antiemesis (Minutes) in each of the groups.

Figure 13: Association Between Effectiveness and Onset of Antiemesis (Minutes)

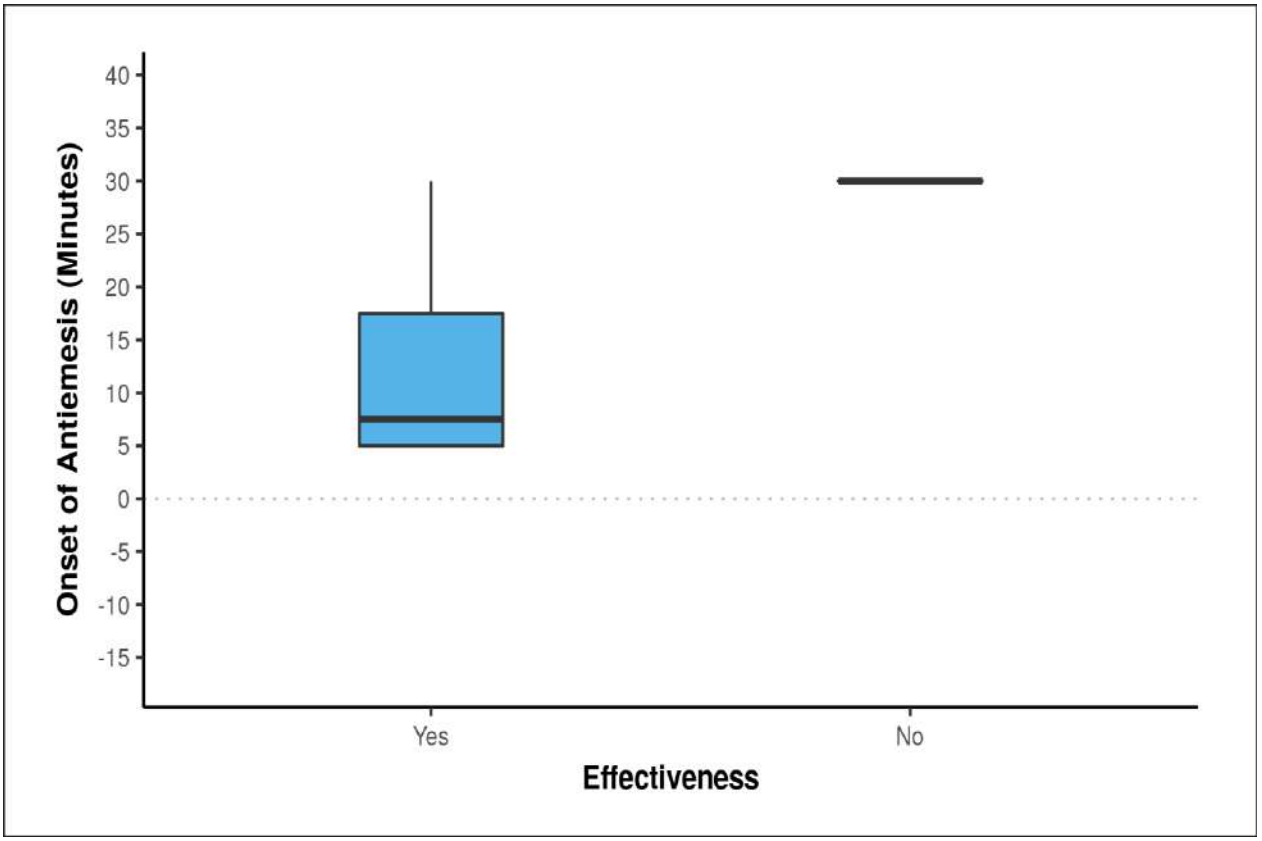
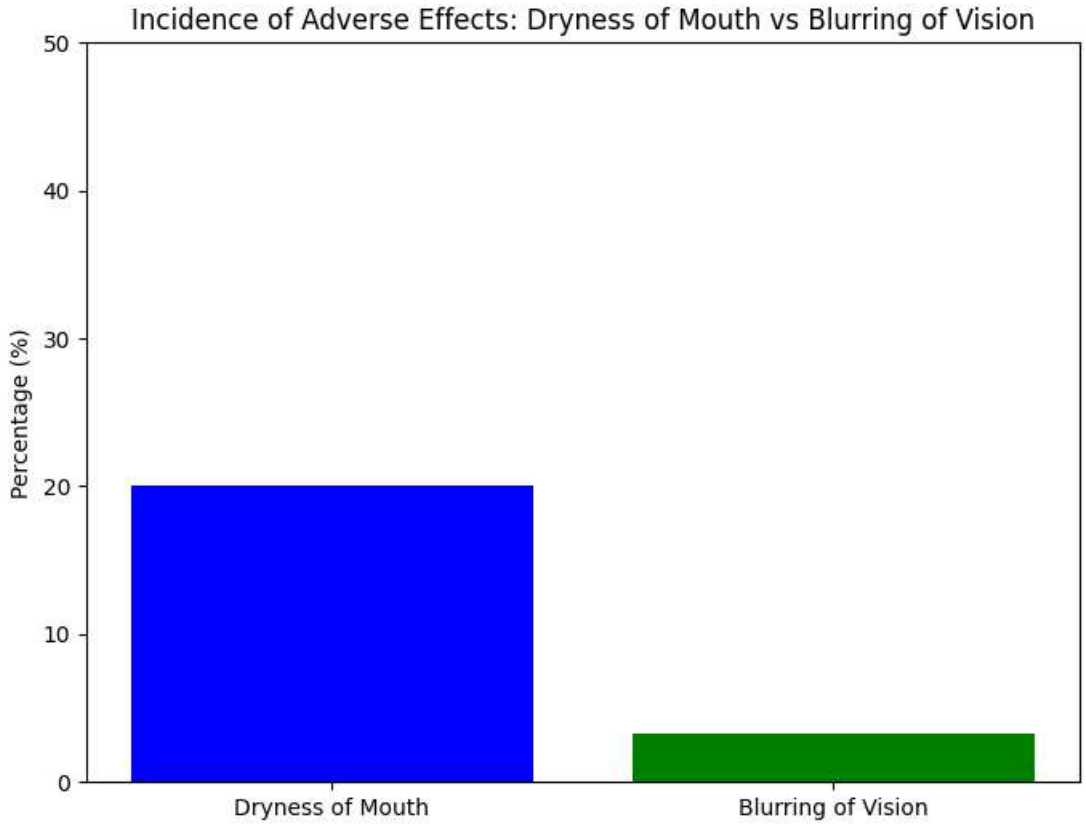


Table 14: Summary of Adverse effects

Adverse Effects	Yes	No
Dryness Of Mouth	12 (20.0%)	48 (80.0%)
Blurring Of Vision	2 (3.3%)	58 (96.6%)

Figure 14: Percentage of adverse effects



12 (20.0%) of the participants had Dryness Of Mouth: Yes. 48 (80.0%) of the participants had Dryness Of Mouth: No.

2 (3.3%) of the participants had Blurring Of Vision: Yes. 58 (96.6%) of the participants had Blurring Of Vision: No.

Table 15: Distribution of the Participants in Terms of 'Dryness Of Mouth'

Dryness Of Mouth	Frequency	Percentage	95% CI
Yes	12	20.0%	10.4% - 29.6%
No	48	80.0%	70.4% - 89.6%

20.0% of the participants had Dryness Of Mouth: Yes. 80.0% of the participants had Dryness Of Mouth: No.

Figure 15: Distribution of Dryness Of Mouth

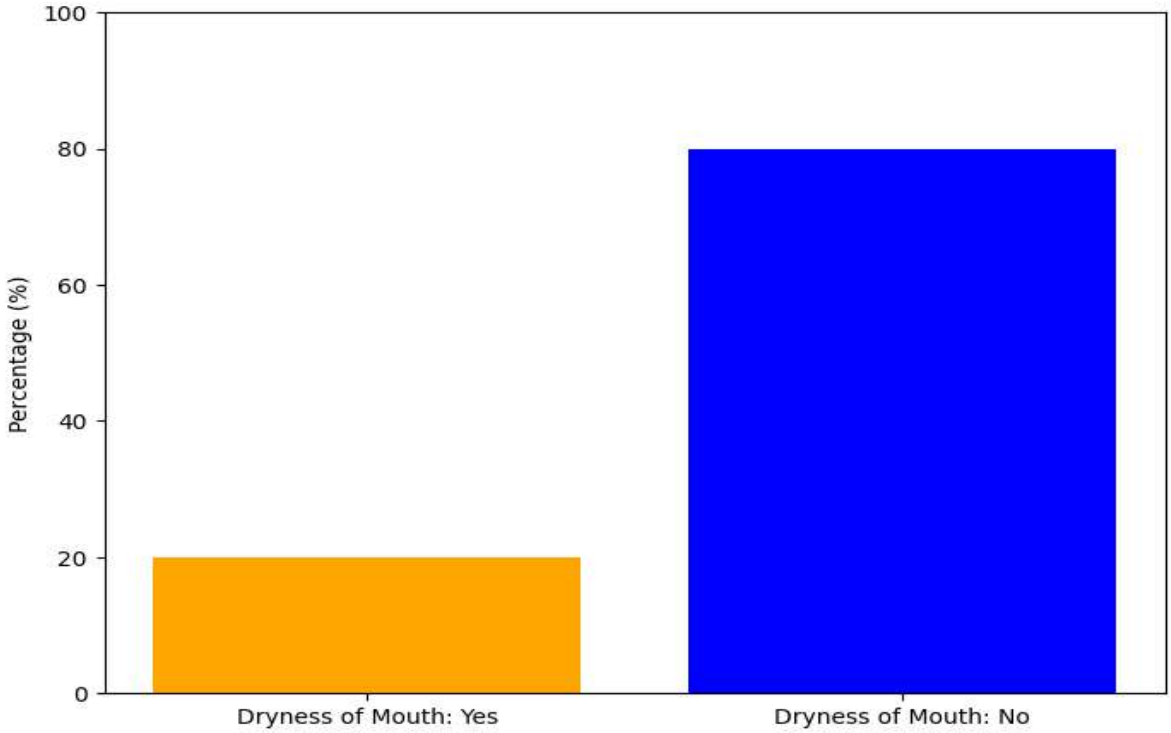
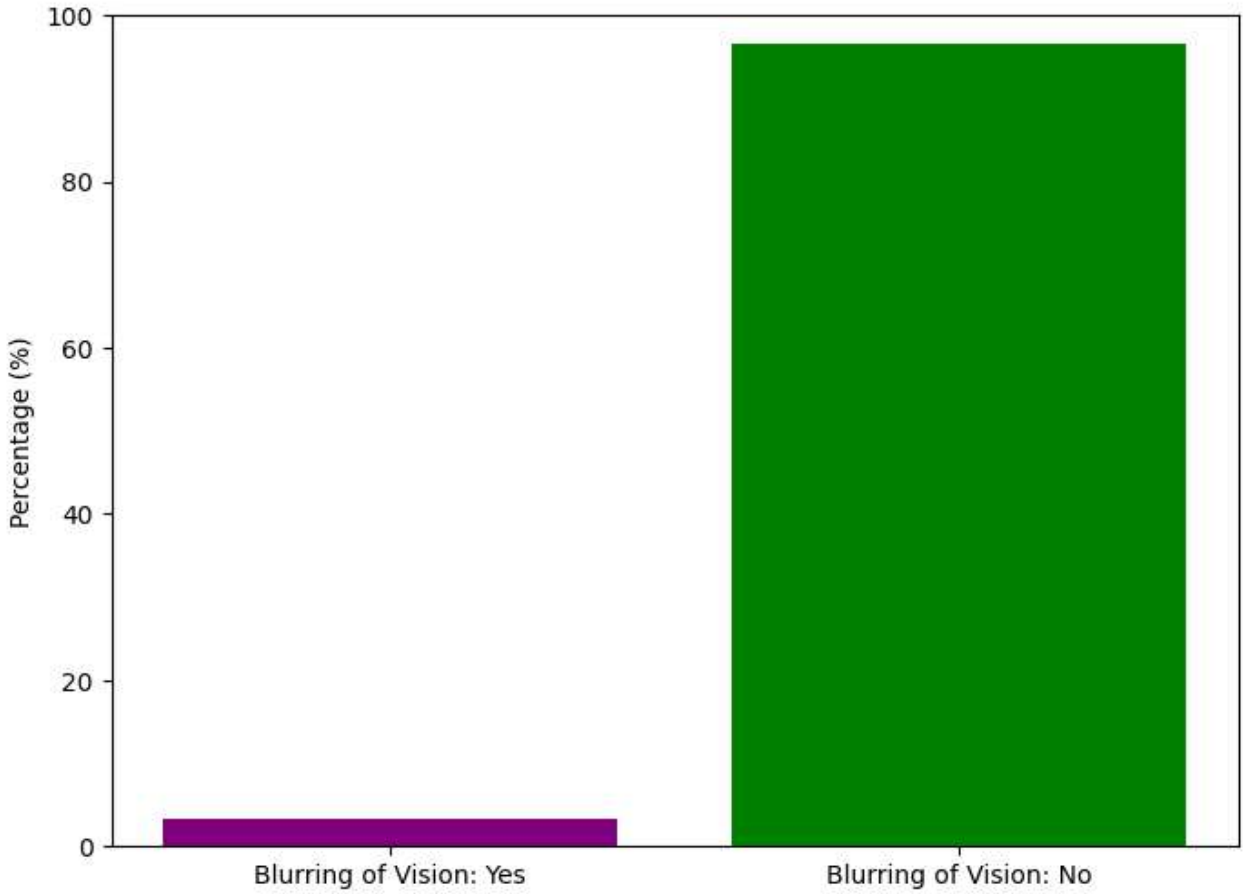


Table 16: Distribution of the Participants in Terms of 'Blurring Of Vision'

Blurring Of Vision	Frequency	Percentage	95% CI
Yes	2	3.3%	0.4% - 11.5%
No	58	96.6%	88.5% - 99.6%

3.3% of the participants had Blurring Of Vision: Yes. 96.6% of the participants had Blurring Of Vision: No.

Figure 16: Distribution of Blurring Of Vision



Discussion

The primary aim of this study was to evaluate the effectiveness of intravenous atropine in treating nausea and vomiting associated with spinal anesthesia in parturient females undergoing elective cesarean section. The findings of this study demonstrated that intravenous atropine significantly reduced nausea and vomiting as measured by the Visual Analogue Scale (VAS), showing a reduction from a mean baseline score of 8.63 to 0.80 within 120 minutes post-administration.

This observed effect aligns with previous studies that have highlighted atropine's vagolytic properties as a mechanism for reducing nausea and vomiting during spinal anesthesia. For instance, **Santos et al**. and **Ward et al**. both reported significant reductions in nausea and vomiting when atropine was administered during spinal anesthesia (7) (12). Similarly, the findings in our study are consistent with those of **Ure et al.** , who demonstrated that preoperative glycopyrrolate, a similar anticholinergic, reduced the incidence and severity of nausea and vomiting without adverse effects on neonates. (17)

However, despite the significant reduction in nausea and vomiting, it is worth noting that some patients continued to experience symptoms, albeit at lower intensities, even after atropine administration. This outcome reflects the multifactorial etiology of intraoperative nausea and vomiting (IONV) in cesarean sections under spinal anesthesia. Factors such as hypotension, visceral manipulation, and the use of uterotonic agents remain contributory, as indicated by Jelting et al. who underscored the importance of managing circulatory parameters to minimize these symptoms. (5)

The mean VAS score dropped from 8.63 at baseline to 0.80 at 120 minutes post-administration, indicating a rapid and sustained reduction in symptoms. This is particularly noteworthy as the antiemetic effects were maintained throughout the entire 120-minute observation period. These findings are consistent with previous studies, such as **Ward et al**. which demonstrated that atropine is effective in reducing nausea and vomiting associated with high spinal anesthesia. (12) In terms of onset of antiemetic action, the mean onset time for nausea and vomiting relief was 13.36 minutes, with a multimodal distribution suggesting that individual patient responses to atropine varied significantly. This variation could be due to underlying physiological differences, including the degree of spinal block achieved and individual sensitivity to atropine. Previous studies have suggested that antiemetic onset varies depending on the dosage and individual patient characteristics (**Vadhanan et al.**).

Despite the efficacy demonstrated in this study, it is important to contextualize these findings within the broader literature. Atropine, while effective, is not without its limitations. Concerns regarding its side effects, such as tachycardia and dry mouth, are well-documented (**Santos et al.**) (7). Moreover, while atropine performed well in this study, comparison with other antiemetic agents, such as ondansetron and dexamethasone, may be warranted to determine the most effective regimen for minimizing IONV in obstetric populations (**Wang et al.**)

The hemodynamic parameters in our study resulted in a statistically significant increase in systolic and diastolic blood pressure, as well as mean arterial pressure (MAP). The baseline systolic blood pressure was recorded at 107.22 mmHg, which increased to 117.68 mmHg at 120 minutes post-administration. Similarly, diastolic blood pressure increased from 65.78 mmHg at baseline to 74.80 mmHg at 120 minutes, and MAP increased from 79.59 mmHg at

baseline to 89.09 mmHg. These changes were significant, indicating that atropine effectively counteracted the hypotensive effects of spinal anesthesia. Atropine also had a notable effect on heart rate. The mean heart rate increased from 85.92 beats per minute (bpm) at baseline to 95.17 bpm at 5 minutes post-administration, then gradually returned to 89.60 bpm by 120 minutes. This increase in heart rate reflects atropine's well-known vagolytic effect, which counteracts bradycardia caused by parasympathetic dominance during spinal anaesthesia. These observations are consistent with findings by **Abdalla et al.** , who reported that atropine's vagolytic effects help manage bradycardia and hypotension caused by spinal anesthesia. (10) Notably, there was no evidence of severe adverse effects such as extreme tachycardia, suggesting that atropine administration in the context of this study was safe and well-tolerated by the patients. Nonetheless, the gradual stabilization of heart rate by the 120-minute mark may indicate that while atropine is effective, its effects are transient, necessitating careful monitoring throughout the postoperative period.

Ondansetron is one of the most widely studied and used antiemetic agents in obstetric anesthesia, particularly during spinal anesthesia for cesarean sections. The literature, including studies by **Abouleish et al.** and **Charbit et al.** , highlights ondansetron's effectiveness in reducing nausea and vomiting. Abouleish et al. reported a significant reduction in the incidence of vomiting when ondansetron was administered post-umbilical cord clamping during elective cesarean sections, reducing vomiting from 58% in the placebo group to 36% in the treatment group. (9) Moreover, ondansetron was shown to reduce the severity of nausea, though the study did not observe a significant reduction in its incidence, which is a point of divergence from the findings in this study, where atropine not only reduced nausea severity but also lowered its incidence considerably. (9)

In contrast, **Czarnetzki et al.** explored ondansetron's efficacy as a prophylactic agent for nausea and vomiting during spinal anesthesia and reported similar findings. However, their results also indicated that while ondansetron was effective in reducing nausea, it often did not prevent hypotension, a major trigger for nausea during spinal anesthesia. This is where atropine may have an advantage, as evidenced in your study, where the administration of atropine not only reduced nausea but also contributed to a more stable hemodynamic profile by increasing systolic and diastolic blood pressure, counteracting spinal anesthesia-induced hypotension. This suggests that atropine's dual action of both vagolytic and antiemetic effects could provide a more comprehensive solution for managing nausea and vomiting compared to ondansetron, which primarily acts on serotonin receptors but does not mitigate hypotension.

The side-effect profile is another crucial consideration. While ondansetron is generally well-tolerated, there are concerns about its long-term use, particularly regarding QT interval prolongation, which can lead to arrhythmias. **Charbit et al.** emphasized this concern, making ondansetron less favorable for repeated use, especially in high-risk populations such as obstetric patients. Atropine, on the other hand, is not associated with these cardiac risks, although it does carry its own side effects, such as dry mouth and potential tachycardia. In this study, no adverse events like extreme tachycardia were observed, suggesting that 0.4mg atropine may be a safer alternative to treat the multifactorial nausea and vomiting in parturient undergoing caesarean.

Dexamethasone is another agent frequently explored in the literature as an antiemetic, particularly in combination with other drugs. The study by **Abdalla et al.** provides insight into the use of dexamethasone combined with intrathecal atropine for preventing nausea and

vomiting related to morphine use in spinal anesthesia. (10) Their study compared three groups: dexamethasone alone, atropine alone, and a combination of both. The group receiving the combination of dexamethasone and atropine experienced the lowest incidence of both nausea and vomiting, suggesting a synergistic effect when these drugs are used together. (10)

In comparison to our study, which focused on atropine alone, Abdalla's results support the idea that while atropine is effective as a monotherapy, its combination with other agents like dexamethasone could potentially enhance its antiemetic efficacy. However, it is important to note that the combination therapy may also introduce additional side effects. In Abdalla's study, patients receiving the combination therapy did not report significant adverse effects, but the potential for dexamethasone-induced hyperglycemia, immunosuppression, and other corticosteroid-related side effects must be considered when evaluating the broader applicability of this regimen.

Dexamethasone's long-lasting antiemetic effect—extending up to 24 hours—also contrasts with the relatively quicker onset but shorter duration of atropine's antiemetic properties observed in your study. This suggests that while atropine provides rapid relief, dexamethasone might be more appropriate for long-term nausea management, particularly in settings where nausea may persist beyond the immediate postoperative period. Nevertheless, our study demonstrated that atropine's rapid onset within 5 minutes was highly beneficial during the acute phases of cesarean delivery, making it particularly suited for intraoperative use where immediate control of symptoms is necessary.

Metoclopramide, a dopamine antagonist, is another antiemetic frequently discussed in the literature. In studies like those conducted by **Lussos et al.** and **Jabalmeli et al.** , metoclopramide was found to significantly reduce nausea and vomiting when administered before the induction of spinal anesthesia. (8) (18) **Lussos et al.** showed that metoclopramide reduced the incidence of nausea and vomiting from 81% to 14% in the treatment (8)

Glycopyrrolate, another anticholinergic agent, has been investigated for its potential to reduce nausea and vomiting by preventing bradycardia and hypotension. **Ure et al.** conducted a study comparing glycopyrrolate with a placebo in preventing nausea and vomiting during spinal anaesthesia for caesarean sections. (17) The study found that glycopyrrolate significantly reduced the incidence and severity of nausea, as well as the requirement for ephedrine to treat hypotension. Glycopyrrolate, like atropine, prevents parasympathetic activation, but its use is limited by its side effects, which can include dry mouth and difficulty in visual accommodation. (17)

Atropine and glycopyrrolate have similar mechanisms of action, both being anticholinergic agents that block vagal activity. However, atropine has a faster onset of action, which is beneficial in acute settings where rapid symptom relief is needed. Glycopyrrolate, on the other hand, is longer-acting but may not be as effective when immediate intervention is required, such as in cases of intraoperative nausea and vomiting. (17) Furthermore, glycopyrrolate does not cross the blood-brain barrier, limiting its effectiveness in treating central causes of nausea, whereas atropine, which can penetrate the central nervous system, may offer broader antiemetic benefits. However, atropine’s central action also means it has a higher likelihood of causing confusion or delirium in some patients, particularly at higher doses, which is less of a concern with glycopyrrolate. (17)

DISCUSSION

Droperidol, a dopamine receptor antagonist, was once a common choice for preventing nausea and vomiting in caesarean sections. **Santos et al.** demonstrated that droperidol significantly reduced the incidence of nausea (12% in the droperidol group vs. 40% in the control group) and completely eliminated vomiting in treated patients. (7) However, droperidol use has declined due to concerns about its potential to cause QT interval prolongation and the risk of torsades de pointes, a potentially life-threatening arrhythmia. (7) Atropine does not carry the same risk of QT prolongation, making it a safer option for patients at risk of arrhythmias. Furthermore, droperidol's sedative properties may not be desirable. (7)

Jabalmeli et al. studied the effects of midazolam, either alone or in combination with ondansetron, in preventing nausea and vomiting during spinal anaesthesia. Midazolam's antiemetic effects are thought to stem from its sedative properties, which reduce anxiety and visceral discomfort. However, like ondansetron and dexamethasone, midazolam does not have a direct effect on blood pressure or heart rate. (18) In contrast, atropine's role as a muscarinic receptor antagonist allows it to directly influence heart rate and blood pressure by counteracting vagal stimulation. In the current study, atropine produced a significant increase in heart rate, helping to reverse the bradycardia commonly seen in spinal anaesthesia. Midazolam, while effective in reducing anxiety-related nausea, lacks this ability to stabilize hemodynamics, making it less effective in cases where nausea is caused by hypotension or bradycardia. (18)

In our study, atropine was generally well tolerated, with relatively few adverse effects. The most commonly reported side effect was dry mouth, observed in 20.0% of participants, consistent with the known anticholinergic properties of atropine, which inhibit saliva

production, leading to dryness in the oral cavity. Blurring of vision, a less frequent side effect, was reported in 3.3% of participants. This occurs due to atropine's effect on the eye muscles, particularly its ability to dilate pupils and reduce accommodation, leading to temporary vision disturbances.

These adverse effects are typical of muscarinic receptor antagonists and were expected based on atropine's pharmacological profile. The incidence of these side effects, although mild, was moderate and did not pose a significant barrier to the overall use of atropine in the study population.(20) It is important to note that although these effects were mild, they may still cause discomfort for some patients, particularly in prolonged surgical procedures or when higher doses of atropine are required.(20)

Compared to **Libersa et al.** where similar adverse reactions were observed, particularly dry mouth and visual disturbances, our findings align with their study. Libersa et al. found a significant occurrence of dry mouth in patients, especially at higher doses of atropine. In contrast to their study, where tachycardia was a more frequent and sometimes clinically significant adverse event, no severe cases of tachycardia were reported in our study.(20) This could be attributed to the lower controlled dose of atropine used in our population. Additionally, while Libersa et al. reported cases of urinary retention and constipation, these side effects were not observed in our study, possibly due to the different patient demographics and controlled perioperative environment of pregnant women undergoing cesarean sections (20).

Summary

The goal of the research is to determine how well intravenous atropine works for treating nausea and vomiting brought on by spinal anaesthesia in female parturient having elective cesarean sections. The quick onset, ease of use, and efficiency of spinal anaesthetic in preventing sensory blockage while preserving mother consciousness have led to its widespread use. However, IONV is a frequent side effect of spinal anesthesia, especially in cases of LSCS. various causes like spinal induced sympathetic blockade-induced hypotension, vagal hyperactivity, and the use of uterotonic drugs, are implicated in these symptoms. Atropine, a muscarinic antagonist, has previously been suggested as an effective treatment for vagally mediated bradycardia and hypotension, which are common triggers for nausea and vomiting during high spinal anesthesia.

A longitudinal, single-arm observational study design was employed, where 60 pregnant female as sample size undergoing elective lower-segment cesarean sections studied. Reduction in VAS scores for nausea and vomiting after intravenous atropine administration were observed as primary objective. Secondary outcomes included hemodynamic changes, specifically systolic and diastolic blood pressure, heart rate, and the duration of atropine's antiemetic effects.

The results indicated a significant reduction in nausea and vomiting post-administration of atropine. The mean VAS score for nausea decreased from 8.63 at baseline to 0.23 at 120

minutes after atropine administration, demonstrating rapid and sustained symptom relief. Hemodynamic stability was also observed, with significant rise in SBP, DBP and MAP. Additionally, HR increased shortly after atropine administration, proving its vagolytic effects.

The study's findings are in line with the past research, such as Ward et al. (1966) and Santos et al. (1984), which highlighted atropine's effectiveness in reducing IONV during spinal anesthesia. The rapid onset of action—an average of 13.36 minutes for the onset of antiemetic effects—makes atropine particularly beneficial in acute settings where quick symptom relief is required.

In addition to being useful in treating nausea and vomiting, atropine was also well-tolerated by patients; no serious side effects, such as excessive tachycardia or dry mouth, were noted. Atropine resulted in stabilization of the hemodynamic parameters as opposed to ondansetron and dexamethasone which prevents nausea and vomiting but do not lead to stabilization of hemodynamic parameters.

Conclusion

In this study, intravenous atropine provided a viable solution for managing intra-operative nausea and vomiting associated with spinal anesthesia in parturient undergoing cesarean sections. Its dual action of providing both antiemetic relief and improving hemodynamic stability makes it a unique and valuable to add in antiemetic protocols for obstetric patients. However, further multicenter, large sample size research comparing atropine with other antiemetic agents is warranted to confirm the external validity of these findings and to add the atropine in antiemetic protocol in parturient undergoing caesarean.

Limitations

Our study had some limitations too

1) Single tertiary care centre, which may limit the generalizability of the findings to other settings or populations.
2) This was a single-arm observational study, and the lack of a control group receiving either a placebo or an alternative antiemetic limits the ability to compare atropine's efficacy directly with other treatments.
3) Also, our sample size for the study was small.
4) Blinding could not be implemented because of limited trained personnels.

Future scope of research: In future a comparison study of iv atropine with other antiemetic agents may be planned. In this study a placebo arm should also be kept as control.

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Appendix

Observation chart

Name:

Age:

CR No.:

Date:

Diagnosis:

History of preceding antiemetic before spinal anaesthesia(Y/N):

Amount of bupivacaine given in spinal anaesthesia:

Sensory level achieved:

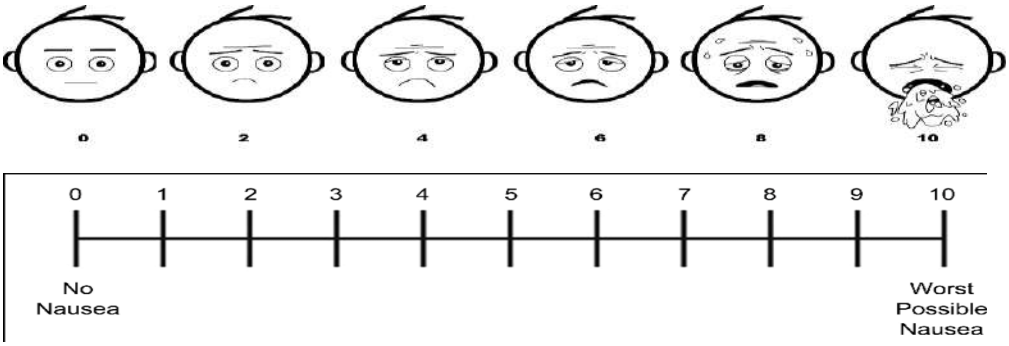
Duration from spinal anaesthesia till cord clamping:

VAS of nausea before atropine administration:

Amount of atropine administered:

Changes in VAS of nausea, heart rate and blood pressure after atropine administration:

	Baseline	5min	10min	20min	30min	60min	120min
VAS of nausea							
Heart rate							
Blood pressure							



Rescue drug (ondansetron) given (Y/N): If (Y), then amount of ondansetron given:

Dryness of mouth (Y/N): Blurring of vision (Y/N):

Appendix

Participant Information Sheet

1. **Study Title:** Efficacy of intravenous atropine to treat nausea and vomiting associated with spinal anaesthesia in patients undergoing elective caesarean section
2. **Study Investigators:**
    - **Student:** Dr. Abhinav Vijay, Department of Anaesthesiology and Critical Care
    - **Guide:** Dr. J.P. Sharma, Department of Anaesthesiology and Critical Care
    - **Co guide:** Dr. Molli Kiran, Department of Anaesthesiology and Critical Care
3. **Introduction:** We are conducting a research study to find the effectiveness of intravenous atropine in reducing the nausea and vomiting in patients of spinal anaesthesia undergoing caesarean section. Caesarean section is a very common surgery being performed and spinal anaesthesia is being employed very commonly resulting to complain of nausea and vomiting. Atropine has been given as the drug of choice for this but its efficacy still remains unevaluated. We will be conducting this study in hope to find efficacy of atropine in the mentioned regard. if you wish to participate voluntarily then we will ask you to sign a consent form.
4. **Purpose of the study:**
   the aim of our study is to find the efficacy of intravenous atropine in reducing nausea and vomiting (via visual analog scale of nausea) in patients of spinal anaesthesia undergoing caesarean section. This will help us find the efficacy of atropine in the mentioned regard. This will also help us know how atropine changes the hemodynamic parameters in the given situation.
5. **Taking part what it involves:**
   i) **Do I have to take part?**
   Participation in this research is entirely voluntary. A decision to not take part, or to withdraw at any time, will not affect your rights or medical care in any way
   ii) **What is expected of me if I take part?**
   If you participate, during the procedure you will be asked if you are having any problem related to nausea and vomiting and if you complain so then 0.4 mg intravenous atropine will be given to you as mentioned the Miller's textbook of anaesthesia, and your decrease in nausea and vomiting will be evaluated via the visual analog scale of nausea
   iii) **How long will my part in study last?**
   Your participation in study will last as long as the surgery goes on. Once the baby is out and cord has been clamped you will be given atropine as an antiemetic only if you complain of nausea or vomiting. Response to the medication will be assessed quickly and via visual analog scale of nausea effectiveness of the medication will be assessed. Once you will be shifted from the operation theatre the research study will end.
   iv) **What are the possible benefits in taking part?**

Taking part in the study will lead to close monitoring of any kind of discomfort felt by you during the surgery and actions will be taken for ensuring safe and smooth procedure. Taking part will help gain knowledge in efficacy of intravenous atropine in reducing nausea and vomiting in spinal anaesthesia, which may result in better management of nausea and vomiting intraoperatively.

v) **What are the possible disadvantage and risks of taking part?**
There are no major foreseeable disadvantages or risks because of the study. There may be risk of loss of privacy and confidentiality of information collected even though all possible measures will be taken to ensure safe data storage and access.

vi) **What happens to the Information collected from me?**
All information collected will be kept strictly confidential and not shared with anyone. Results from the study will be reported as group data and will not identify you in any way.

vii) **What if I change my mind regarding participation in the study?**
You are entitled to change your mind and withdraw at any time during the study without any disadvantage or penalty.

viii) **Whom do I contact for more information or if I have further questions or concerns?**
If you want any information or have questions or concerns, you can contact:

Dr. Abhinav Vijay
Post graduate student
Department of Anaesthesiology and
Critical Care, AIIMS Bhopal
(9509950265, gmonu3998@gmail.com)

भागीदारी सूचना पत्र

1.**अध्ययन शीर्षक:** ऐच्छिक सिजेरियन सेक्शन से गुजर रहे रोगियों में स्पाइनल एनेस्थीसिया से जुड़ी मतली और उल्टी के इलाज के लिए अंतःशिरा एट्रोपिन की प्रभावकारिता

2.**अध्ययन अन्वेषक:**

• **छात्र:** डॉ. अभिनव विजय, एनेस्थिसियोलॉजी और क्रिटिकल केयर विभाग

• **मार्गदर्शक:** डॉ. जे.पी. शर्मा, एनेस्थिसियोलॉजी और क्रिटिकल केयर विभाग

• **सह मार्गदर्शक:** डॉ. मोली किरण, एनेस्थिसियोलॉजी और क्रिटिकल केयर विभाग

3.**परिचय:**

हम सिजेरियन सेक्शन से गुजर रहे स्पाइनल एनेस्थीसिया के रोगियों में मतली और उल्टी को कम करने में अंतःशिरा एट्रोपिन की प्रभावशीलता का पता लगाने के लिए एक शोध अध्ययन कर रहे हैं। सिजेरियन सेक्शन एक बहुत ही सामान्य सर्जरी की जा रही है और स्पाइनल एनेस्थीसिया का उपयोग किया जा रहा है जिसके परिणामस्वरूप आमतौर पर मतली और उल्टी की शिकायत होती है। इसके लिए एट्रोपिन को पसंद की दवा के रूप में दिया गया है लेकिन इसकी प्रभावकारिता का अभी भी मूल्यांकन नहीं किया गया है। हम उल्लेखित संबंध में एट्रोपिन की प्रभावकारिता खोजने की आशा में यह अध्ययन कर रहे हैं। यदि आप स्वेच्छा से भाग लेना चाहते हैं तो हम आपसे सहमति फॉर्म पर हस्ताक्षर करने के लिए कहेंगे।

4. **अध्ययन का उद्देश्य:**

हमारे अध्ययन का उद्देश्य सिजेरियन सेक्शन से गुजर रहे स्पाइनल एनेस्थीसिया के रोगियों में मतली और उल्टी (मतली के दृश्य अनुरूप पैमाने के माध्यम से) को कम करने में अंतःशिरा एट्रोपिन की प्रभावकारिता का पता लगाना है। यह हमें उल्लिखित संबंध में एट्रोपिन की प्रभावकारिता का पता लगाने में मदद करेगा। इससे हमें यह जानने में भी मदद मिलेगी कि दी गई स्थिति में एट्रोपिन हेमोडायनामिक मापदंडों को कैसे बदलता है।

5. **इसमें क्या शामिल है भाग लेना:**

i) **क्या मुझे भाग लेना है?**

इस शोध में भागीदारी पूरी तरह से स्वैच्छिक है। भाग न लेने या किसी भी समय वापस लेने का निर्णय किसी भी तरह से आपके अधिकारों या चिकित्सा देखभाल को प्रभावित नहीं करेगा

ii) **यदि मैं भाग लेता हूँ तो मुझसे क्या अपेक्षा की जाती है?**

यदि आप भाग लेते हैं, तो प्रक्रिया के दौरान आपसे पूछा जाएगा कि क्या आपको मतली और उल्टी से संबंधित कोई समस्या हो रही है और यदि आप ऐसी शिकायत करते हैं तो 0.4 मिलीग्राम अंतःशिरा एट्रोपिन आपको दिया जाएगा जैसा कि मिलर की एनेस्थीसिया की पाठ्यपुस्तक में बताया गया है, और मतली में आपकी कमी और उल्टी का मूल्यांकन मतली के दृश्य अनुरूप पैमाने के माध्यम से किया जाएगा

iii) **अध्ययन में मेरा हिस्सा कितने समय तक चलेगा?**

अध्ययन में आपकी भागीदारी तब तक रहेगी जब तक सर्जरी चलती रहेगी। एक बार जब बच्चा बाहर हो जाता है और गर्भनाल को जकड़ दिया जाता है, तो आपको मतली या उल्टी की शिकायत होने पर ही आपको एंटीमैटिक के रूप में एट्रोपिन दिया जाएगा। दवा के प्रति प्रतिक्रिया का जल्दी से मूल्यांकन किया जाएगा और मतली के दृश्य अनुरूप पैमाने के माध्यम से दवा की प्रभावशीलता का आकलन किया जाएगा। एक बार जब आपको ऑपरेशन थिएटर से स्थानांतरित कर दिया जाएगा तो शोध अध्ययन समाप्त हो जाएगा।

iv) **भाग लेने के संभावित लाभ क्या हैं?**

अध्ययन में भाग लेने से सर्जरी के दौरान आपके द्वारा महसूस की गई किसी भी प्रकार की असुविधा की बारीकी से निगरानी की जाएगी और सुरक्षित और सुचारू प्रक्रिया सुनिश्चित करने के लिए कार्रवाई की जाएगी। भाग लेने से की प्रभावकारिता में ज्ञान प्राप्त करने में मदद मिलेगी

स्पाइनल एनेस्थीसिया में मतली और उल्टी को कम करने में अंतःशिरा एट्रोपिन, जिसके परिणामस्वरूप अंतःक्रियात्मक रूप से मतली और उल्टी का बेहतर प्रबंधन हो सकता है।

v) **भाग लेने के संभावित नुकसान और जोखिम क्या हैं?**

अध्ययन की वजह से कोई बड़ा अनुमानित नुकसान या जोखिम नहीं हैं। एकत्र की गई जानकारी की गोपनीयता और गोपनीयता के नुकसान का जोखिम हो सकता है, भले ही सुरक्षित डेटा भंडारण और पहुंच सुनिश्चित करने के लिए सभी संभव उपाय किए जाएंगे।

vi) **मुझसे एकत्र की गई जानकारी का क्या होता है?**

एकत्र की गई सभी सूचनाओं को कड़ाई से गोपनीय रखा जाएगा और किसी के साथ साझा नहीं किया जाएगा। अध्ययन के परिणाम समूह डेटा के रूप में रिपोर्ट किए जाएंगे और किसी भी तरह से आपकी पहचान नहीं करेंगे।

vii) **यदि मैं अध्ययन में भाग लेने के बारे में अपना विचार बदल दूं तो क्या होगा?**

आप अपना विचार बदलने और अध्ययन के दौरान किसी भी समय बिना किसी नुकसान या दंड के वापस लेने के हकदार हैं।

viii) **अधिक जानकारी के लिए या यदि मेरे पास और प्रश्न या चिंताएँ हैं, तो मैं किससे संपर्क करूँ?**

Appendix

यदि आप कोई जानकारी चाहते हैं या आपके कोई प्रश्न या चिंताएँ हैं, तो आप संपर्क कर सकते हैं:

डॉ अभिनव विजय

स्नातकोत्तर विद्यार्थी

एनेस्थिसियोलॉजी विभाग और

क्रिटिकल केयर, एम्स भोपाल

(9509950265, gmonu3998@gmail.com)

Appendix

प्रतिभागी सूचना सहमति प्रपत

Participant Information Consent Form

अध्ययन के लिए प्रतिभागी का पहचान नंबर / Participant identification number for the study ……

……

अनुसंधान का शीर्षक / Title of research: ऐच्छिक सिजेरियन सेक्शन से गुजर रहे रोगियों में स्पाइनल एनेस्थीसिया से जुड़ी मतली और उल्टी के इलाज के लिए अंतःशिरा एट्रोपिन की प्रभावकारिता / Efficacy of intravenous atropine to treat nausea and vomiting associated with spinal anaesthesia in patients undergoing elective caesarean section

छात्र शोधकिाष का नाम / Name of student investigator: डॉ अभिनव विजय / Dr. Abhinav Vijay

शोध मागषदशषक का नामName of thesis guide / : डॉ. जे.पी. शर्मा / Dr. J.P. Sharma

सूचना पत्र की सामग्री दिनांक 14/01/2023 थी बशर्ते मेरे द्वारा ध्यानपूर्वक पढ़ा गया हो/मुझे विस्तार से समझाया गया हो, उस भाषा में जिसे मैं समझता हूं, और मैंने पूरी तरह से समझा है / सामग्री को समझा। मैं पुष्टि करता हूं कि मुझे प्रश्न पूछने का अवसर मिला है। The contents of the information sheet dated 14/01/2023 that was provided have been read carefully by me / explained in detail to me, in a language that comprehend, and I have fully understood the contents. I confirm that I have had the opportunity to ask questions.

अध्ययन की प्रकृति और उद्देश्य और इसके संभावित जोखिम/लाभ और अध्ययन की अपेक्षित अवधि, और अध्ययन के अन्य प्रासंगिक विवरण दिए गए हैं मुझे विस्तार से समझाया। मैं समझता हूं कि मेरी भागीदारी स्वैच्छिक है और मैं किसी भी समय अपना नाम वापस लेने के लिए स्वतंत्र हूं, बिना कोई कारण बताए, मेरी चिकित्सा देखभाल या कानूनी अधिकार प्रभावित हुए बिना / The nature and purpose of the study and its potential risks/benefits and expected duration of the study, and other relevant details of the study have been explained to me in detail. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal right being affected

मैं समझता हूं कि मेरे द्वारा मेरे बारे में जानकारी एकत्र की गई है इस शोध में भागीदारी और मेरे किसी भी मेडिकल नोट के अनुभागों को जिम्मेदार व्यक्तियों द्वारा देखा जा सकता है एम्स। मैं इन व्यक्तियों को मेरे रिकॉर्ड तक पहुंच की अनुमति देता हूं। / I understand that the information collected about me from my participation in this research and sections of any of my medical notes may be looked at by

responsible individuals from AIIMS. I give permission for these individuals to have access to my records.

मैं उपरोक्त अध्ययन में भाग लेने के लिए सहमत हूं। / I agree to take part in the above study.

☐

_✕_____

(हस्ताक्षर / बाएं अंगूठे का निशान) / (Signature / Left Thumb Impression)

दिनांक/Date…….. स्थान/Place……

प्रतिभागी का नाम / Name of the participant ……

पिता/पति/पत्नी का नाम / Son/Daughter/Spouse of…….

डाक का पूरा पता / Complete postal address …….

अगर अनपढ़/ if illiterate

सूचना पत्रक को पढ़ा जाता है और प्रतिभागी को समझाया जाता है, और प्रश्न पूछने का अवसर दिया जाता है। मैं इस बात की पुष्टि करता हूँ कि व्यक्ति ने स्वतंत्र रूप से सहमति दी है।

The information sheet has been read and explained to the participant, and given the opportunity to ask questions. I confirm that the individual has given consent freely.

कानूनी रूप से स्वीकार्य प्रतिनिधि या निष्पक्ष गवाह के हस्ताक्षर:

Signature of Legally Acceptable Representative or impartial witness:

दिनांक / Date:

एलएआर या निष्पक्ष गवाह का नाम / Name of LAR or impartial witness:

पता / Address …….

यह प्रमाणित किया जाता है कि उपरोक्त सहमति मेरी उपस्थिति में प्राप्त की गई है।

This is to certify that the above consent has been obtained in my presence

…….

Appendix

	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W
1	Age	Preceding Antiemetic	Weight (Kg)	Height (cm)	BMI (Kg/m²)	BMI	Amount Of Atropine	Systolic BP (mmHg) (Baseline)	Systolic BP (mmHg) (5 Minutes)	Systolic BP (mmHg) (10 Minutes)	Systolic BP (mmHg) (20 Minutes)	Systolic BP (mmHg) (30 Minutes)	Systolic BP (mmHg) (60 Minutes)	Systolic BP (mmHg) (120 Minutes)	Diastolic BP (mmHg) (Baseline)	Diastolic BP (mmHg) (5 Minutes)	Diastolic BP (mmHg) (10 Minutes)	Diastolic BP (mmHg) (20 Minutes)	Diastolic BP (mmHg) (30 Minutes)	Diastolic BP (mmHg) (60 Minutes)	Diastolic BP (mmHg) (120 Minutes)	
2	20-29 Years	No	78	160	30.47	30.0-34.9 Kg/m2	0.4mg	104	119	115	110	112	109	114	62	64	60	67	63	66	71	
3	30-39 Years	No	55	154	23.19	23.0-24.9 Kg/m2	0.4mg	100	121	119	120	110	112	117	62	50	57	54	67	59	67	
4	20-29 Years	No	67	163	25.22	25.0-29.9 Kg/m2	0.4mg	105	115	99	110	107	120	121	67	65	68	64	62	72	73	
5	30-39 Years	No	83	157	33.64	30.0-34.9 Kg/m2	0.4mg	104	110	114	113	124	110	126	62	67	68	60	57	69	72	
6	20-29 Years	No	60	150	26.67	25.0-29.9 Kg/m2	0.4mg	143	146	138	140	155	154	146	96	109	98	90	111	101	98	
7	30-39 Years	No	71	170	24.57	23.0-24.9 Kg/m2	0.4mg	115	114	110	110	92	96	98	82	78	69	76	68	67	72	
8	20-29 Years	No	88	158	35.27	35.0-39.9 Kg/m2	0.4mg	104	110	110	108	106	108	110	70	80	82	80	74	80	80	
9	30-39 Years	No	53	152	22.94	18.5-22.9 Kg/m2	0.4mg	111	109	134	121	126	124	112	75	49	68	69	81	83	82	
10	20-29 Years	No	62	161	23.92	23.0-24.9 Kg/m2	0.4mg	106	110	102	110	108	115	109	68	70	78	68	62	72	71	
11	20-29 Years	No	79	155	32.85	30.0-34.9 Kg/m2	0.4mg	108	110	115	99	100	115	114	62	74	70	65	62	72	80	
12	20-29 Years	No	65	162	24.77	23.0-24.9 Kg/m2	0.4mg	110	120	118	110	108	108	120	58	64	62	65	72	68	68	
13	20-29 Years	No	72	159	28.45	25.0-29.9 Kg/m2	0.4mg	101	110	115	110	110	112	115	58	62	70	60	58	64	75	
14	30-39 Years	No	50	151	21.94	18.5-22.9 Kg/m2	0.4mg	110	109	115	112	105	110	115	70	67	65	68	72	67	70	
15	20-29 Years	No	85	164	31.6	30.0-34.9 Kg/m2	0.4mg	110	124	120	119	127	130	118	65	70	70	68	69	70	74	
16	30-39 Years	No	59	153	25.18	25.0-29.9 Kg/m2	0.4mg	110	120	126	118	117	124	118	62	80	82	78	69	92	74	
17	20-29 Years	No	77	160	30.08	30.0-34.9 Kg/m2	0.4mg	110	118	115	112	117	110	115	65	70	68	73	70	70	74	
18	30-39 Years	No	58	150	25.78	25.0-29.9 Kg/m2	0.4mg	90	115	120	118	98	95	110	65	70	75	75	70	74	78	
19	20-29 Years	No	86	170	29.75	25.0-29.9 Kg/m2	0.4mg	98	105	99	90	97	110	112	60	65	62	64	59	62	65	
20	30-39 Years	No	66	158	26.46	25.0-29.9 Kg/m2	0.4mg	92	99	101	99	100	110	120	65	70	64	62	59	65	72	
21	20-29 Years	No	80	152	34.59	30.0-34.9 Kg/m2	0.4mg	120	130	129	126	128	118	125	75	88	70	70	80	84	83	
22	20-29 Years	No	56	154	23.62	23.0-24.9 Kg/m2	0.4mg	112	120	118	112	115	120	108	68	80	78	74	80	70	68	
23	20-29 Years	No	70	161	27.01	25.0-29.9 Kg/m2	0.4mg	102	105	111	110	118	105	120	70	68	70	68	70	70	70	
24	20-29 Years	No	74	163	27.85	25.0-29.9 Kg/m2	0.4mg	112	108	110	115	114	118	120	68	70	60	70	76	80	75	
25	20-29 Years	No	68	157	27.63	25.0-29.9 Kg/m2	0.4mg	110	112	108	120	118	109	119	64	70	68	70	65	73	71	
26	30-39 Years	No	62	151	27.22	25.0-29.9 Kg/m2	0.4mg	105	110	115	102	110	115	114	58	68	65	60	70	71	68	
27	30-39 Years	No	82	162	31.23	30.0-34.9 Kg/m2	0.4mg	110	115	112	115	120	116	124	68	72	74	77	81	78	70	
28	30-39 Years	No	60	160	23.44	23.0-24.9 Kg/m2	0.4mg	105	110	112	111	110	112	115	64	60	74	64	68	71	77	
29	20-29 Years	No	84	164	31.22	30.0-34.9 Kg/m2	0.4mg	118	120	116	120	114	116	111	62	58	65	70	68	63	72	
30	20-29 Years	No	53	155	22.06	18.5-22.9 Kg/m2	0.4mg	110	112	115	114	120	116	118	70	68	72	73	70	77	80	
31	30-39 Years	No	75	159	29.67	25.0-29.9 Kg/m2	0.4mg	108	105	103	107	110	112	115	62	70	68	65	70	72	75	
32	20-29 Years	No	90	170	31.14	30.0-34.9 Kg/m2	0.4mg	111	98	115	102	120	118	120	67	70	75	70	72	62	72	
33	30-39 Years	No	69	152	29.88	25.0-29.9 Kg/m2	0.4mg	100	105	110	112	108	110	110	60	65	60	70	65	72	68	
34	30-39 Years	No	57	158	22.83	18.5-22.9 Kg/m2	0.4mg	100	120	118	115	114	118	126	52	65	68	70	72	69	86	
35	20-29 Years	No	64	150	28.44	25.0-29.9 Kg/m2	0.4mg	99	100	98	110	108	111	118	59	60	58	64	60	65	68	
36	20-29 Years	No	73	161	28.14	25.0-29.9 Kg/m2	0.4mg	108	105	110	105	112	108	118	64	70	64	62	70	76	78	
37	20-29 Years	No	61	153	26.05	25.0-29.9 Kg/m2	0.4mg	113	110	115	112	105	110	115	68	70	74	70	77	73	78	
38	20-29 Years	No	87	162	33.17	30.0-34.9 Kg/m2	0.4mg	112	128	130	121	126	130	124	58	68	70	72	78	81	82	
39	20-29 Years	No	52	155	21.63	18.5-22.9 Kg/m2	0.4mg	90	98	100	105	109	110	126	68	65	68	70	76	68	78	
40	30-39 Years	No	81	160	31.64	30.0-34.9 Kg/m2	0.4mg	125	118	122	121	130	128	125	70	72	73	70	81	72	85	
41	20-29 Years	No	59	157	23.93	23.0-24.9 Kg/m2	0.4mg	112	115	110	126	118	110	115	67	70	65	72	68	74	77	
42	20-29 Years	No	76	151	33.29	30.0-34.9 Kg/m2	0.4mg	118	115	116	118	108	120	123	60	62	76	65	70	72	79	
43	20-29 Years	No	63	164	23.43	23.0-24.9 Kg/m2	0.4mg	92	105	103	107	110	109	115	60	72	67	65	70	69	74	
44	30-39 Years	No	67	163	25.22	25.0-29.9 Kg/m2	0.4mg	90	99	94	110	111	109	110	59	62	67	72	71	67	76	
45	20-29 Years	No	55	150	24.44	23.0-24.9 Kg/m2	0.4mg	101	115	118	107	119	127	111	60	65	58	67	70	71	69	
46	20-29 Years	No	79	162	30.1	30.0-34.9 Kg/m2	0.4mg	102	112	111	120	116	117	122	68	68	59	68	59	63	62	
47	20-29 Years	No	83	158	33.3	30.0-34.9 Kg/m2	0.4mg	97	109	111	105	111	103	117	71	72	70	65	68	71	75	
48	30-39 Years	No	54	159	21.37	18.5-22.9 Kg/m2	0.4mg	115	114	110	108	103	113	119	71	68	59	66	65	71	62	
49	20-29 Years	No	66	152	28.57	25.0-29.9 Kg/m2	0.4mg	104	102	111	118	119	108	111	64	59	60	68	72	68	67	
50	20-29 Years	No	89	170	30.8	30.0-34.9 Kg/m2	0.4mg	99	98	105	101	100	112	114	59	65	67	72	68	74	70	
51	30-39 Years	No	71	160	27.73	25.0-29.9 Kg/m2	0.4mg	114	123	118	115	105	116	125	70	71	84	74	75	73	71	
52	30-39 Years	No	58	154	24.47	23.0-24.9 Kg/m2	0.4mg	110	118	120	113	105	119	109	58	65	64	71	78	71	79	
53	30-39 Years	No	82	157	33.28	30.0-34.9 Kg/m2	0.4mg	106	118	112	116	113	103	126	68	74	80	72	71	78	83	
54	20-29 Years	No	74	153	31.59	30.0-34.9 Kg/m2	0.4mg	110	112	123	119	109	114	127	72	84	73	71	85	81	81	
55	20-29 Years	No	61	151	26.75	25.0-29.9 Kg/m2	0.4mg	108	105	110	109	119	112	116	68	67	65	63	61	72	74	
56	30-39 Years	No	77	162	29.35	25.0-29.9 Kg/m2	0.4mg	107	117	111	109	112	117	123	87	74	76	79	81	83	75	
57	20-29 Years	No	64	158	25.64	25.0-29.9 Kg/m2	0.4mg	101	112	115	108	118	121	116	69	65	75	72	77	83	77	
58	30-39 Years	No	69	164	25.64	25.0-29.9 Kg/m2	0.4mg	110	109	113	109	112	114	118	64	71	67	71	68	62	75	
59	30-39 Years	No	53	150	23.56	23.0-24.9 Kg/m2	0.4mg	118	128	119	121	115	117	123	65	74	84	78	85	71	82	
60	20-29 Years	No	85	155	35.41	35.0-39.9 Kg/m2	0.4mg	108	112	113	119	126	115	125	58	68	69	78	79	84	85	
61	30-39 Years	No	72	163	27.1	25.0-29.9 Kg/m2	0.4mg	110	122	120	118	121	110	115	60	72	73	69	71	69	75	

Appendix

	X	Y	Z	AA	AB	AC	AD	AE	AF	AG	AH	AI	AJ	AK	AL	AM	AN	AO	AP	AQ	AR	AS	AT	AU	AV
1	MAP (mmHg) (Baseline)	MAP (mmHg) (5 Minutes)	MAP (mmHg) (10 Minutes)	MAP (mmHg) (20 Minutes)	MAP (mmHg) (30 Minutes)	MAP (mmHg) (60 Minutes)	MAP (mmHg) (120 Minutes)	Heart Rate (BPM) (Baseline)	Heart Rate (BPM) (5 Minutes)	Heart Rate (BPM) (10 Minutes)	Heart Rate (BPM) (20 Minutes)	Heart Rate (BPM) (30 Minutes)	Heart Rate (BPM) (60 Minutes)	Heart Rate (BPM) (120 Minutes)	VAS for Nausea/Vomiting (Baseline)	VAS for Nausea/Vomiting (5 Minutes)	VAS for Nausea/Vomiting (10 Minutes)	VAS for Nausea/Vomiting (20 Minutes)	VAS for Nausea/Vomiting (30 Minutes)	VAS for Nausea/Vomiting (60 Minutes)	VAS for Nausea/Vomiting (120 Minutes)	VAS >4 for Nausea/Vomiting (Baseline)	VAS >4 for Nausea/Vomiting (5 Minutes)	VAS >4 for Nausea/Vomiting (10 Minutes)	VAS >4 for Nausea/Vomiting (20 Minutes)
2	76	82	78	81	79	80	85	86	102	98	96	88	94	89	9	3	0	0	0	0	0	Yes	No	No	No
3	75	74	78	76	81	77	84	87	113	110	112	97	101	94	8	4	2	0	0	0	0	Yes	Yes	No	No
4	80	82	78	79	77	88	89	95	110	112	108	110	101	99	10	8	2	0	0	0	0	Yes	Yes	No	No
5	76	81	83	78	79	83	90	75	124	126	118	107	99	98	9	0	0	0	0	4	4	Yes	No	No	No
6	112	121	111	107	126	119	114	98	128	129	146	131	112	115	10	6	0	0	0	0	0	Yes	Yes	No	No
7	93	90	83	87	76	77	81	105	110	108	107	114	104	110	10	6	0	0	0	0	2	Yes	Yes	No	No
8	81	90	91	89	85	89	90	84	105	101	98	100	94	92	8	4	2	0	0	0	0	Yes	Yes	No	No
9	87	69	90	86	96	97	92	85	105	97	100	103	81	84	8	2	0	0	0	0	0	Yes	No	No	No
10	81	83	86	82	77	86	84	78	88	90	92	88	84	94	10	4	2	0	0	0	0	Yes	Yes	No	No
11	77	86	85	76	75	86	91	78	87	88	90	82	80	90	8	2	0	0	0	2	4	Yes	No	No	No
12	75	83	81	80	84	81	85	64	75	68	69	70	73	66	8	0	0	0	0	0	0	Yes	No	No	No
13	72	78	85	77	75	80	88	90	101	92	88	92	78	90	10	0	0	0	0	0	0	Yes	No	No	No
14	83	81	82	83	83	81	85	78	80	80	76	84	73	85	8	2	0	0	0	0	0	Yes	No	No	No
15	80	88	87	85	88	90	89	112	119	110	115	120	117	118	8	6	6	4	2	2	2	Yes	Yes	Yes	Yes
16	78	93	97	91	85	103	89	82	112	115	108	102	96	92	7	5	2	0	0	0	0	Yes	Yes	No	No
17	80	86	84	86	86	83	88	90	105	101	95	96	90	94	8	0	0	0	0	0	0	Yes	No	No	No
18	73	85	90	89	79	81	89	87	120	127	132	128	117	115	9	6	6	5	5	5	5	Yes	Yes	Yes	Yes
19	73	78	74	73	72	78	81	67	75	80	68	74	75	80	9	4	2	2	0	0	0	Yes	Yes	No	No
20	74	80	76	74	73	80	88	87	90	77	86	83	78	80	8	0	0	0	0	0	0	Yes	No	No	No
21	90	102	90	89	96	95	97	110	128	130	115	102	108	105	8	6	2	2	0	0	0	Yes	Yes	No	No
22	83	93	91	87	92	87	81	88	92	89	102	87	95	80	9	4	2	2	2	2	2	Yes	Yes	No	No
23	81	80	84	82	86	82	87	92	112	95	90	88	85	82	7	0	0	0	0	0	0	Yes	No	No	No
24	83	83	77	85	89	93	90	90	88	96	87	94	92	88	10	5	5	0	0	0	0	Yes	Yes	Yes	No
25	79	84	81	87	83	85	87	77	84	80	78	85	90	88	7	2	0	0	0	0	2	Yes	No	No	No
26	74	82	82	74	83	86	83	101	98	90	80	92	94	88	8	5	2	0	0	0	0	Yes	Yes	No	No
27	82	86	87	90	94	91	88	105	115	108	119	99	95	92	10	5	5	5	2	2	0	Yes	Yes	Yes	Yes
28	78	77	87	80	82	85	90	85	78	80	87	90	83	91	6	0	0	0	0	0	2	Yes	No	No	No
29	81	79	82	87	83	81	85	78	82	75	70	82	75	78	8	4	2	0	0	0	0	Yes	Yes	No	No
30	83	83	86	87	87	90	93	62	68	66	72	65	63	67	10	0	0	0	0	0	2	Yes	No	No	No
31	77	82	80	79	83	85	88	85	92	106	95	87	92	90	9	2	0	0	0	0	0	Yes	No	No	No
32	82	79	88	81	88	81	88	76	80	77	75	82	70	84	7	0	0	0	0	0	0	Yes	No	No	No
33	73	78	77	84	79	85	82	87	83	92	90	84	87	90	6	0	0	0	0	0	0	Yes	No	No	No
34	68	83	85	85	86	85	99	95	105	112	110	114	108	111	8	6	4	2	0	0	4	Yes	Yes	Yes	No
35	72	73	71	79	76	80	85	86	80	92	101	87	90	95	7	3	0	0	0	0	0	Yes	No	No	No
36	79	82	79	76	84	87	91	89	84	90	87	88	82	83	8	0	0	0	0	0	2	Yes	No	No	No
37	83	83	88	84	86	85	90	99	104	95	105	98	101	97	8	0	0	0	0	0	0	Yes	No	No	No
38	76	88	90	88	94	97	96	78	89	91	88	93	79	87	10	0	0	0	0	0	0	Yes	No	No	No
39	75	76	79	82	87	82	94	80	84	92	81	78	87	86	7	2	0	0	0	0	0	Yes	No	No	No
40	88	87	89	87	97	91	98	80	85	90	78	97	87	91	6	0	0	0	0	0	0	Yes	No	No	No
41	82	85	80	90	85	86	90	74	84	75	87	92	72	95	7	2	0	0	0	2	2	Yes	No	No	No
42	79	80	89	83	83	88	94	68	74	78	80	75	77	79	10	0	0	0	0	0	0	Yes	No	No	No
43	71	83	79	79	83	82	86	107	103	111	105	116	118	97	8	0	0	0	0	0	0	Yes	No	No	No
44	69	74	76	85	84	81	87	111	118	105	103	118	108	99	10	4	4	2	2	0	2	Yes	Yes	Yes	No
45	74	82	78	80	86	90	83	87	79	92	88	78	95	88	8	2	0	0	0	0	0	Yes	No	No	No
46	79	83	76	85	78	81	82	90	80	82	78	75	78	77	10	0	0	0	0	0	0	Yes	No	No	No
47	80	84	84	78	82	82	89	71	68	75	66	71	72	69	8	5	2	0	0	0	0	Yes	Yes	No	No
48	86	83	76	80	78	85	81	73	87	91	77	89	90	80	7	2	1	1	1	1	1	Yes	No	No	No
49	77	73	77	85	88	81	82	72	85	78	82	68	77	90	8	0	0	0	0	0	0	Yes	No	No	No
50	72	76	80	82	79	87	85	68	82	76	69	70	75	80	10	0	0	0	0	0	0	Yes	No	No	No
51	85	88	95	88	85	87	89	90	82	78	81	75	82	80	10	4	2	2	2	2	2	Yes	Yes	No	No
52	75	83	83	85	87	87	89	103	115	104	102	106	101	95	10	0	0	0	0	0	0	Yes	No	No	No
53	81	89	91	87	85	86	97	78	87	92	88	91	84	86	8	0	0	0	0	0	2	Yes	No	No	No
54	85	93	90	87	93	92	96	90	110	112	99	101	95	92	10	0	0	0	0	0	0	Yes	No	No	No
55	81	80	80	78	80	85	88	77	87	84	76	81	75	72	10	0	0	0	0	0	2	Yes	No	No	No
56	94	88	88	89	91	94	91	79	87	93	78	76	84	74	10	2	2	0	0	0	0	Yes	No	No	No
57	80	81	88	84	91	96	90	78	81	93	79	89	85	92	10	0	0	0	0	2	2	Yes	No	No	No
58	79	84	82	84	83	79	89	101	99	91	87	85	88	92	10	0	0	0	0	0	0	Yes	No	No	No
59	83	92	96	92	95	86	96	79	115	119	122	117	113	98	10	0	0	0	0	0	0	Yes	No	No	No
60	75	83	84	92	95	94	98	115	135	136	127	128	114	113	10	4	0	0	0	0	4	Yes	Yes	No	No
61	77	89	89	85	88	83	88	68	72	65	74	66	72	70	10	0	0	0	0	0	0	Yes	No	No	No

Appendix

	AL	AM	AN	AO	AP	AQ	AR	AS	AT	AU	AV	AW	AX	AY	AZ	BA	BB	BC	BD	BE	BF	BG
1	VAS for Nausea/Vomiting (Baseline)	VAS for Nausea/Vomiting (5 Minutes)	VAS for Nausea/Vomiting (10 Minutes)	VAS for Nausea/Vomiting (20 Minutes)	VAS for Nausea/Vomiting (30 Minutes)	VAS for Nausea/Vomiting (60 Minutes)	VAS for Nausea/Vomiting (120 Minutes)	VAS >4 for Nausea/Vomiting (Baseline)	VAS >4 for Nausea/Vomiting (5 Minutes)	VAS >4 for Nausea/Vomiting (10 Minutes)	VAS >4 for Nausea/Vomiting (20 Minutes)	VAS >4 for Nausea/Vomiting (30 Minutes)	VAS >4 for Nausea/Vomiting (60 Minutes)	VAS >4 for Nausea/Vomiting (120 Minutes)	Onset of Antiemesis (Minutes)	Rescue Drug	Effectiveness	Dryness Of Mouth	Blurring Of Vision			
2	9	3	0	0	0	0	0	Yes	No	No	No	No	No	No	10	Not Required	Yes	No	No			
3	8	4	2	0	0	0	0	Yes	Yes	No	No	No	No	No	20	Not Required	Yes	No	No			
4	10	8	2	0	0	0	0	Yes	Yes	No	No	No	No	No	20	Not Required	Yes	No	No			
5	9	0	0	0	0	4	4	Yes	No	No	No	No	Yes	Yes	5	Not Required	Yes	No	No			
6	10	6	0	0	0	0	0	Yes	Yes	No	No	No	No	No	10	Not Required	Yes	No	No			
7	10	6	0	0	0	0	2	Yes	Yes	No	No	No	No	No	10	Not Required	Yes	Yes	No			
8	8	4	2	0	0	0	0	Yes	Yes	No	No	No	No	No	20	Not Required	Yes	No	No			
9	8	2	0	0	0	0	0	Yes	No	No	No	No	No	No	10	Not Required	Yes	No	No			
10	10	4	2	0	0	0	0	Yes	Yes	No	No	No	No	No	20	Not Required	Yes	Yes	No			
11	8	2	0	0	0	2	4	Yes	No	No	No	No	No	Yes	10	Not Required	Yes	No	No			
12	8	0	0	0	0	0	0	Yes	No	No	No	No	No	No	5	Not Required	Yes	No	No			
13	10	0	0	0	0	0	0	Yes	No	No	No	No	No	No	5	Not Required	Yes	No	No			
14	8	2	0	0	0	0	0	Yes	No	No	No	No	No	No	10	Not Required	Yes	No	No			
15	8	6	6	4	2	2	2	Yes	Yes	Yes	Yes	No	No	No		Not Required	Yes	No	No			
16	7	5	2	0	0	0	0	Yes	Yes	No	No	No	No	No	20	Not Required	Yes	No	No			
17	8	0	0	0	0	0	0	Yes	No	No	No	No	No	No	5	Not Required	Yes	No	No			
18	9	6	6	5	5	5	5	Yes	Yes	Yes	Yes	Yes	Yes	Yes		Required	No	No	No			
19	9	4	2	2	0	0	0	Yes	Yes	No	No	No	No	No	30	Not Required	Yes	No	No			
20	8	0	0	0	0	0	0	Yes	No	No	No	No	No	No	5	Not Required	Yes	Yes	Yes			
21	8	6	2	2	0	0	0	Yes	Yes	No	No	No	No	No	30	Not Required	Yes	No	No			
22	9	4	2	2	2	2	2	Yes	Yes	No	No	No	No	No		Not Required	Yes	Yes	No			
23	7	0	0	0	0	0	0	Yes	No	No	No	No	No	No	5	Not Required	Yes	No	No			
24	10	5	5	0	0	0	0	Yes	Yes	Yes	No	No	No	No	20	Not Required	Yes	No	No			
25	7	2	0	0	0	0	2	Yes	No	No	No	No	No	No	10	Not Required	Yes	Yes	No			
26	8	5	2	0	0	0	0	Yes	Yes	No	No	No	No	No	20	Not Required	Yes	No	No			
27	10	5	5	5	2	2	0	Yes	Yes	Yes	Yes	No	No	No	120	Not Required	Yes	No	No			
28	6	0	0	0	0	0	2	Yes	No	No	No	No	No	No	5	Not Required	Yes	No	No			
29	8	4	2	0	0	0	0	Yes	Yes	No	No	No	No	No	20	Not Required	Yes	No	No			
30	10	0	0	0	0	0	2	Yes	No	No	No	No	No	No	5	Not Required	Yes	Yes	No			
31	9	2	0	0	0	0	0	Yes	No	No	No	No	No	No	10	Not Required	Yes	No	No			
32	7	0	0	0	0	0	0	Yes	No	No	No	No	No	No	5	Not Required	Yes	No	No			
33	6	0	0	0	0	0	0	Yes	No	No	No	No	No	No	5	Not Required	Yes	Yes	No			
34	8	6	4	2	0	0	4	Yes	Yes	Yes	No	No	No	Yes	30	Required	No	No	No			
35	7	3	0	0	0	0	0	Yes	No	No	No	No	No	No	10	Not Required	Yes	No	No			
36	8	0	0	0	0	0	2	Yes	No	No	No	No	No	No	5	Not Required	Yes	No	No			
37	8	0	0	0	0	0	0	Yes	No	No	No	No	No	No	5	Not Required	Yes	Yes	No			
38	10	0	0	0	0	0	0	Yes	No	No	No	No	No	No	5	Not Required	Yes	No	No			
39	7	2	0	0	0	0	0	Yes	No	No	No	No	No	No	10	Not Required	Yes	No	No			
40	6	0	0	0	0	0	0	Yes	No	No	No	No	No	No	5	Not Required	Yes	No	No			
41	7	2	0	0	0	2	2	Yes	No	No	No	No	No	No	10	Not Required	Yes	No	No			
42	10	0	0	0	0	0	0	Yes	No	No	No	No	No	No	5	Not Required	Yes	Yes	No			
43	8	0	0	0	0	0	0	Yes	No	No	No	No	No	No	5	Not Required	Yes	No	No			
44	10	4	4	2	2	0	2	Yes	Yes	Yes	No	No	No	No	60	Not Required	Yes	No	No			
45	8	2	0	0	0	0	0	Yes	No	No	No	No	No	No	10	Not Required	Yes	No	No			
46	10	0	0	0	0	0	0	Yes	No	No	No	No	No	No	5	Not Required	Yes	No	No			
47	8	5	2	0	0	0	0	Yes	Yes	No	No	No	No	No	20	Not Required	Yes	No	No			
48	7	2	1	1	1	1	1	Yes	No	No	No	No	No	No		Not Required	Yes	Yes	Yes			
49	8	0	0	0	0	0	0	Yes	No	No	No	No	No	No	5	Not Required	Yes	No	No			
50	10	0	0	0	0	0	0	Yes	No	No	No	No	No	No	5	Not Required	Yes	No	No			
51	10	4	2	2	2	2	2	Yes	Yes	No	No	No	No	No		Not Required	Yes	No	No			
52	10	0	0	0	0	0	0	Yes	No	No	No	No	No	No	5	Not Required	Yes	Yes	No			
53	8	0	0	0	0	0	2	Yes	No	No	No	No	No	No	5	Not Required	Yes	No	No			
54	10	0	0	0	0	0	0	Yes	No	No	No	No	No	No	5	Not Required	Yes	No	No			
55	10	0	0	0	0	0	2	Yes	No	No	No	No	No	No	5	Not Required	Yes	No	No			
56	10	2	2	0	0	0	0	Yes	No	No	No	No	No	No	20	Not Required	Yes	No	No			
57	10	0	0	0	0	2	2	Yes	No	No	No	No	No	No	5	Not Required	Yes	Yes	No			
58	10	0	0	0	0	0	0	Yes	No	No	No	No	No	No	5	Not Required	Yes	No	No			
59	10	0	0	0	0	0	0	Yes	No	No	No	No	No	No	5	Not Required	Yes	No	No			
60	10	4	0	0	0	0	4	Yes	Yes	No	No	No	No	Yes	10	Not Required	Yes	No	No			
61	10	0	0	0	0	0	0	Yes	No	No	No	No	No	No	5	Not Required	Yes	No	No			

Appendix